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L16  ANSWER 1 OF 19  HCAPLUS  COPYRIGHT 2006 ACS on STN
AN   2006:495296  HCAPLUS
DN   145:41322
ED   Entered STN:  26 May 2006
TI   Estimation of uncertainty in the detection of bacterial endotoxin by the
     gel-clot method
AU   Lourenco, Filipe; Kaneko, Telma Mary; Pinto, Terezinha de Jesus Andreoli
CS   Departmento de Farmacia, Faculdade de Ciencias Farmaceuticas, Universidade
     de Sao Paulo, Sao Paulo, 05508-900, Brazil
SO   Revista Brasileira de Ciencias Farmaceuticas (2005), 41(4), 437-443
     CODEN: RBCFFM; ISSN: 1516-9332
PB   Universidade de Sao Paulo, Faculdade de Ciencias Farmaceuticas
DT   Journal
LA   Portuguese
CC   4-1 (Toxicology)
AB   Since the publication of ISO 17025:1999, the interest in methods for estimation
     of the uncertainty in qual. anal., such as pass/fail, have became more
     important.  The usual form of estimating and informing the uncertainty in this
     kind of anal. is the use of false-response rates, particularly false-pos.
     and false-neg., determinated from Bayes theorem.  The aim of this paper is
     to establish a method for the estimation of the uncertainty in the detection of
     bacterial endotoxins by in vitro Limulus Amebocyte Lysate (LAL) test.
     Considering the confirmation of LAL sensitivity and the validation of the
     test, the probability of a false-response corresponds to the sum of
     false-neg. and false-pos. result probabilities.  From results obtained was
     verified that the confirmation of LAL sensitivity contributed to the
     uncertainty in a more significant way (67.6%) than the validation of the
     test (32.4%).  Through this simple procedure and data obtained from the
     confirmation of LAL sensibility and the validation of the test it is
     possible to obtain a reasonable estimation of the uncertainty of the detection
     of bacterial endotoxins by gel-clot test.
ST   bacteria endotoxin detn gel clot method uncertainty
IT   Toxins
     RL: ANT (Analyte); ANST (Analytical study)
        (endotoxins; estimation of uncertainty in detection of bacterial
        endotoxin by gel-clot method)
IT   Endotoxemia
       Limulus polyphemus
     Uncertainty principle
```

(estimation of uncertainty in detection of bacterial endotoxin by gel-clot method)
RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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(10) International Organization For Standardization; 1999, ISO/IEC 17025
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L16 ANSWER 2 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN
AN **2006:379450** HCAPLUS
DN 144:482296
ED Entered STN: 26 Apr 2006
TI A rapid highly-sensitive endotoxin detection system
AU Ong, Keat G.; Leland, Joshua M.; Zeng, Kefeng; Barrett, Gary; Zourob, Mohammed; Grimes, Craig A.
CS Department of Electrical Engineering, Department of Materials Science and Engineering, 217 Materials Research Laboratory, The Pennsylvania State University, University Park, PA, 16802, USA
SO Biosensors & Bioelectronics (2006), 21(12), 2270-2274
CODEN: BBIOE4; ISSN: 0956-5663
PB Elsevier B.V.
DT Journal
LA English
CC 4-1 (Toxicology)
AB This paper presents a rapid, highly-sensitive, and low-cost method of endotoxin quantification based on the use of stress-responsive magnetoelastic sensors, that monitor the gel formation (viscosity change) of the Limulus Amoebocyte Lysate (LAL) assay in response to endotoxin. Ribbon-like magnetoelastic sensors, 12.7 mm + 6 mm + 28 μm, were immersed in a LAL assay after mixing with test samples of variable endotoxin concentration, and the decrease in resonance amplitude of the sensor was recorded as a function of time. Exptl. results show excellent correlation between endotoxin concentration and the maximum clot rate, determined by taking the min. point of the first derivative of the amplitude-time curve, as well as the clotting-time, defined as the time that corresponds to the maximum clot rate. Using a LAL gel-clot assay with a sensitivity of 0.06 EU/mL (EU: endotoxin unit), the magnetoelastic sensor based technol. can detect the presence of endotoxin at 0.0105 EU/mL in test requiring approx. 20 min. Unlike optical methods used for determining endotoxin concentration, the color of the test solution does not impact the magnetoelastic sensor measurement. Due to the small size of the sensor reader electronics and low cost, the magnetoelastic sensor based endotoxin detection system is ideally suited for wide-spread use in endotoxin screening for sepsis prevention.
ST endotoxin magnetoelastic sensor sepsis LAL assay
IT **Limulus polyphemus**
(amoebocyte lysate assay; rapid highly-sensitive endotoxin detection system for sepsis prevention)
IT **Toxins**
RL: **ANT (Analyte)**; ANST (Analytical study)
(**endotoxins**; rapid highly-sensitive **endotoxin**

detection system for sepsis prevention)
IT Magnetic sensors
Magnetoelasticity
Sepsis
(rapid highly-sensitive endotoxin detection system for sepsis prevention)
RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Angus, D; Crit Care Med 2001, V29(7), P1303 MEDLINE
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(8) Exley, A; Gut 1992, V33, P1126 MEDLINE
(9) Fink, M; Sepsis and Multiorgan Failure 1997, P383
(10) Guidet, B; Chest 1994, V106, P1194 MEDLINE
(11) Haishima, Y; J Pharm Biomed Anal 2003, V32(3), P495 HCAPLUS
(12) Jain, M; Sens Actuators A 2002, V100, P63
(13) Kollef, M; Chest J 1997, V112, P173 MEDLINE
(14) Nachum, R; J Clin Microbiol 1985, V21, P759 MEDLINE
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(16) Ong, K; IEEE Trans Magn 2003, V39, P3414 HCAPLUS
(17) Rangel-Frausto, M; Infectionous Disease Clinics of North America 1999, P299 MEDLINE
(18) Shankar, K; Sens Actuators B 2005, V107, P640
(19) Sullivan, J; Appl Microbiol 1974, V28, P1023 HCAPLUS
(20) Williams, K; Endotoxins:Pyrogens LAL Testing, and Depyrogenation, Chapter 10 2001

L16 ANSWER 3 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:449989 HCAPLUS
DN 142:459705
ED Entered STN: 27 May 2005
TI Fluorometric determination of coagulation control substances such as endotoxins using coagulating factors and fluorescent rotors
IN Yaegashi, Yasunori; Fujiwara, Norihide; Inada, Katsuya
PA Japan
SO Jpn. Kokai Tokkyo Koho, 14 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM G01N-0033/86
ICS G01N-0021/64; G01N-0033/579
CC 9-5 (Biochemical Methods)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP2005134259	A2	20050526	2003JP-0371190	20031030 <--
PRAI 2003JP-0371190		20031030		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
JP 2005134259	ICM	G01N-0033/86
	ICS	G01N-0021/64; G01N-0033/579
	IPCI	G01N0033-86 [ICM,7]; G01N0021-64 [ICS,7]; G01N0033-579 [ICS,7]
	IPCR	G01N0021-64 [I,A]; G01N0021-64 [I,C*]; G01N0033-579 [I,A]; G01N0033-579 [I,C*]; G01N0033-86 [I,A]; G01N0033-86 [I,C*]
	FTERM	2G043/AA01; 2G043/AA03; 2G043/BA16; 2G043/CA03; 2G043/CA05; 2G043/DA02; 2G043/EA01; 2G043/FA03; 2G043/GA25; 2G043/GB21; 2G043/KA02; 2G043/KA05; 2G043/NA01; 2G043/NA11; 2G045/AA10; 2G045/AA40; 2G045/DA25; 2G045/FA12; 2G045/FB07; 2G045/FB12;

2G045/GC15

OS MARPAT 142:459705

AB A method for determination of concentration of coagulation control substances contained in solns. involves (1) a step to add fluorescent rotors (substances whose fluorescence intensity is changed according to change in viscosity of a solution around the substances) to the sample solns., (2) a step to add coagulating factors, e.g. Limulus reagent, silkworm plasma reagent, etc. ti the solns., (3) a step to measure change in fluorescence intensity upon addition of the fluorescent rotors, and (4) a step to calculate concentration of the coagulation control substances based on the change. The coagulation control substances may be endotoxins, β-D-glucan, peptide glycans, or substances which inhibit coagulation, e.g. antibodies to endotoxins. The fluorescence rotors may be benzene-condensed N-heterocycles (Markush structure given).

ST endotoxin fluorometry Limulus test reagent fluorescent rotor; glucan peptide glycan detn coagulating substance fluorescent rotor

IT **Toxins**
RL: **ANT (Analyte)**; ANST (Analytical study)
(**endotoxins**; fluorometric determination of coagulation control substances, e.g. **endotoxins**, β-D-glucan, or peptide glycans, using fluorescent rotors and coagulating factors, e.g. contained in Limulus test reagents or silkworm plasma)

IT Bombyx mori
Coagulation
Fluorescent indicators
Fluorometry
Limulus polyphemus
(fluorometric determination of coagulation control substances, e.g. endotoxins, β-D-glucan, or peptide glycans, using fluorescent rotors and coagulating factors, e.g. contained in Limulus test reagents or silkworm plasma)

IT Glycopeptides
RL: ANT (Analyte); ANST (Analytical study)
(fluorometric determination of coagulation control substances, e.g. endotoxins, β-D-glucan, or peptide glycans, using fluorescent rotors and coagulating factors, e.g. contained in Limulus test reagents or silkworm plasma)

IT 9041-22-9, β-D-Glucan
RL: ANT (Analyte); ANST (Analytical study)
(fluorometric determination of coagulation control substances, e.g. endotoxins, β-D-glucan, or peptide glycans, using fluorescent rotors and coagulating factors, e.g. contained in Limulus test reagents or silkworm plasma)

L16 ANSWER 4 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:283179 HCAPLUS
DN 142:322969
ED Entered STN: 01 Apr 2005
TI Kit for detecting endotoxin
IN **Castro, Carlos A.; Ridge, Richard J.; Novitsky, Thomas J.**
PA Associates of **Cape Cod**, Inc., USA
SO U.S. Pat. Appl. Publ., 12 pp., Cont.-in-part of U.S. Ser. No. 867,162.
CODEN: USXXCO
DT Patent
LA English
IC ICM C12Q-0001/04
ICS C12Q-0001/34
INCL 435034000
CC 64-1 (Pharmaceutical Analysis)
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US2005069972	A1	20050331	2004US-0897979	20040723 <--
	US2005026239	A1	20050203	2004US-0826922	20040419 <--

US2005048655 A1 20050303 2004US-0867162 20040614 <--
PRAI 2003US-463737P P 20030418 <--
2004US-0826922 A2 20040419 <--
2004US-0867162 A2 20040614

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2005069972	ICM	C12Q-0001/04
	ICS	C12Q-0001/34
	INCL	435034000
	IPCI	C12Q0001-04 [ICM,7]; C12Q0001-34 [ICS,7]
	IPCR	C12Q0001-04 [I,A]; C12Q0001-04 [I,C*]; C12Q0001-34 [I,A]; C12Q0001-34 [I,C*]
	NCL	435/034.000
US2005026239	IPCI	C12Q0001-04 [ICM,7]
	IPCR	C12Q0001-04 [I,A]; C12Q0001-04 [I,C*]; G01N0031-00 [I,A]; G01N0031-00 [I,C*]; G01N0033-554 [I,A]; G01N0033-554 [I,C*]; G01N0033-569 [I,A]; G01N0033-569 [I,C*]
	NCL	435/034.000
US2005048655	IPCI	G01N0033-554 [ICM,7]; G01N0033-569 [ICS,7]; G01N0031-00 [ICS,7]
	IPCR	C12Q0001-04 [I,A]; C12Q0001-04 [I,C*]; G01N0031-00 [I,A]; G01N0031-00 [I,C*]; G01N0033-554 [I,A]; G01N0033-554 [I,C*]; G01N0033-569 [I,A]; G01N0033-569 [I,C*]
	NCL	436/008.000

AB Kits and method for detecting bacterial endotoxin in an aqueous solution are provided. In certain examples, the kit includes at least a first container comprising solid, endotoxin-specific, horseshoe crab amebocyte lysate and at least one buffer, whereby the sensitivity of the amebocyte lysate is pre-certified. In certain examples, the kit also contains at least a second container comprising a defined quantity of endotoxin configured as a pos. product control, wherein the defined quantity of the endotoxin is pre-certified to react pos. with the amebocyte lysate in the first container.

ST endotoxin soln Limulus amebocyte lysate test

IT **Toxins**
RL: **ANT (Analyte)**; ANST (Analytical study)
(**endotoxins**; kit for detecting **endotoxin** in aqueous solns. using Limulus amebocyte lysate-based gel clot assay)

IT Dialysis fluids
Limulus polyphemus
Test kits
(kit for detecting endotoxin in aqueous solns. using Limulus amebocyte lysate-based gel clot assay)

IT Drug delivery systems
(solns.; kit for detecting endotoxin in aqueous solns. using Limulus amebocyte lysate-based gel clot assay)

IT 7732-18-5, Water, analysis
RL: AMX (Analytical matrix); ANST (Analytical study)
(kit for detecting endotoxin in aqueous solns. using Limulus amebocyte lysate-based gel clot assay)

L16 ANSWER 5 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:182302 HCAPLUS
DN 142:246402
ED Entered STN: 04 Mar 2005
TI Kit for detecting endotoxin
IN **Novitsky, Thomas J.; Ridge, Richard J.; Castro, Carlos A.**
PA USA
SO U.S. Pat. Appl. Publ., 12 pp., Cont.-in-part of U.S. Ser. No. 826,922.
CODEN: USXXCO
DT Patent
LA English

IC ICM G01N-0033/554
ICS G01N-0033/569; G01N-0031/00
INCL 436008000
CC 64-1 (Pharmaceutical Analysis)
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US2005048655	A1	20050303	2004US-0867162	20040614 <--
	US2005026239	A1	20050203	2004US-0826922	20040419 <--
	US2005069972	A1	20050331	2004US-0897979	20040723 <--
PRAI	2003US-463737P	P	20030418 <--		
	2004US-0826922	A2	20040419 <--		
	2004US-0867162	A2	20040614		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2005048655	ICM	G01N-0033/554
	ICS	G01N-0033/569; G01N-0031/00
	INCL	436008000
	IPCI	G01N0033-554 [ICM,7]; G01N0033-569 [ICS,7]; G01N0031-00 [ICS,7]
	IPCR	C12Q0001-04 [I,A]; C12Q0001-04 [I,C*]; G01N0031-00 [I,A]; G01N0031-00 [I,C*]; G01N0033-554 [I,A]; G01N0033-554 [I,C*]; G01N0033-569 [I,A]; G01N0033-569 [I,C*]
	NCL	436/008.000
US2005026239	IPCI	C12Q0001-04 [ICM,7]
	IPCR	C12Q0001-04 [I,A]; C12Q0001-04 [I,C*]; G01N0031-00 [I,A]; G01N0031-00 [I,C*]; G01N0033-554 [I,A]; G01N0033-554 [I,C*]; G01N0033-569 [I,A]; G01N0033-569 [I,C*]
	NCL	435/034.000
US2005069972	IPCI	C12Q0001-04 [ICM,7]; C12Q0001-34 [ICS,7]
	IPCR	C12Q0001-04 [I,A]; C12Q0001-04 [I,C*]; C12Q0001-34 [I,A]; C12Q0001-34 [I,C*]
	NCL	435/034.000

AB Kits and method for detecting bacterial endotoxin in an aqueous solution are provided. In certain examples, the kit includes at least a first container comprising solid, endotoxin-specific, horseshoe crab amebocyte lysate, whereby the sensitivity of the amebocyte lysate is pre-certified. In certain examples, the kit also contains at least a second container comprising a defined quantity of endotoxin configured as a pos. product control, wherein the defined quantity of the endotoxin is pre-certified to react pos. with the amebocyte lysate in the first container.

ST kit detecting endotoxin; endotoxin soln Limulus amebocyte lysate test

IT **Toxins**
RL: **ANT (Analyte)**; ANST (Analytical study)
(**endotoxins**; kit for detecting **endotoxin** in aqueous solns. using Limulus amebocyte lysate-based gel clot assay)

IT Dialysis fluids
Limulus polyphemus
Test kits
(kit for detecting endotoxin in aqueous solns. using Limulus amebocyte lysate-based gel clot assay)

IT Drug delivery systems
(solns.; kit for detecting endotoxin in aqueous solns. using Limulus amebocyte lysate-based gel clot assay)

IT 7732-18-5, Water, analysis
RL: AMX (Analytical matrix); ANST (Analytical study)
(kit for detecting endotoxin in aqueous solns. using Limulus amebocyte lysate-based gel clot assay)

L16 ANSWER 6 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:934565 HCAPLUS
DN 141:370698
ED Entered STN: 06 Nov 2004

TI Kit for detecting endotoxin in aqueous solutions
IN **Novitsky, Thomas J.; Ridge, Richard J.; Castro, Carlos A.**
PA Associates of **Cape Cod**, Inc., USA
SO PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM G01N
CC 64-1 (Pharmaceutical Analysis)
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO2004094987	A2	20041104	2004WO-US11917	20040419 <--
	WO2004094987	C1	20041216		
	WO2004094987	A3	20050203		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP---1627040	A2	20060222	2004EP-0750270	20040419 <--
	R: DE, FR, GB, IT, NL				
PRAI	2003US-463737P	P	20030418 <--		
	2004WO-US11917	W	20040419		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2004094987	ICM	G01N
	IPCI	G01N [ICM,7]
	IPCR	C12M0001-34 [I,A]; C12M0001-34 [I,C*]; C12Q0001-04 [I,A]; C12Q0001-04 [I,C*]; C12Q0001-22 [I,A]; C12Q0001-22 [I,C*]; G01N [I,S]; G01N0033-53 [I,A]; G01N0033-53 [I,C*]
EP---1627040	IPCI	C12M0001-34 [ICM,7]; C12Q0001-04 [ICS,7]; C12Q0001-22 [ICS,7]; G01N0033-53 [ICS,7]

AB The present invention relates to a simple, rapid, and cost-effective test kit for specifically detecting bacterial endotoxin in aqueous solns., such as water or dialyzate solns., using a Limulus Amebocyte Lysate (LAL)-based gel clot assay. Advantageously, the test kit can vary in its level of sensitivity for detecting endotoxin. Preferred formulation for the horseshoe crab amebocyte lysate reagent is derived from Limulus polyphemus.

ST endotoxin soln Limulus amebocyte lysate test
IT **Toxins**
RL: **ANT (Analyte)**; ANST (Analytical study)
(**endotoxins**; kit for detecting **endotoxin** in aqueous solns. using Limulus amebocyte lysate-based gel clot assay)
IT Dialysis fluids
Limulus polyphemus
Test kits
(kit for detecting endotoxin in aqueous solns. using Limulus amebocyte lysate-based gel clot assay)
IT Drug delivery systems
(solns.; kit for detecting endotoxin in aqueous solns. using Limulus amebocyte lysate-based gel clot assay)
IT 7732-18-5, Water, analysis
RL: AMX (Analytical matrix); ANST (Analytical study)
(kit for detecting endotoxin in aqueous solns. using Limulus amebocyte lysate-based gel clot assay)

L16 ANSWER 7 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:250233 HCAPLUS
DN 140:267169
ED Entered STN: 26 Mar 2004
TI Development of a compact device for measuring endotoxin concentration by limulus test method
IN Harada, Tokuzo; Hotta, Hiroyuki; Iseki, Yuji; Miura, Kaoru; Takesawa, Shingo; Ishii, Kiyoshi
PA Daisen Membrane Systems Co., Ltd., Japan; Medicalseed Co., Ltd.
SO Jpn. Kokai Tokkyo Koho, 19 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM G01N-0033/579
ICS G01N-0021/03; G01N-0021/11; G01N-0021/75
CC 9-1 (Biochemical Methods)
Section cross-reference(s): 4, 10
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP2004093536	A2	20040325	2002JP-0258939	20020904 <--
PRAI 2002JP-0258939		20020904 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
JP 2004093536	ICM	G01N-0033/579
	ICS	G01N-0021/03; G01N-0021/11; G01N-0021/75
	IPCI	G01N0033-579 [ICM,7]; G01N0021-03 [ICS,7]; G01N0021-11 [ICS,7]; G01N0021-75 [ICS,7]
	IPCR	G01N0021-03 [I,A]; G01N0021-03 [I,C*]; G01N0021-11 [I,A]; G01N0021-11 [I,C*]; G01N0021-75 [I,A]; G01N0021-75 [I,C*]; G01N0033-579 [I,A]; G01N0033-579 [I,C*]
	FTERM	2G054/AB07; 2G054/BB10; 2G054/CA20; 2G054/EA04; 2G054/EB10; 2G054/EB12; 2G054/FA17; 2G054/FA21; 2G054/FA42; 2G054/FA43; 2G054/GA01; 2G054/GB01; 2G054/JA01; 2G054/JA06; 2G054/JA11; 2G057/AA01; 2G057/AB06; 2G057/AC01; 2G057/BA01; 2G057/BB06; 2G057/BB09; 2G057/BC05; 2G057/GA01; 2G057/GA06

AB A simple assay cell device for performing the limulus test for measuring endotoxin concentration just by sample injection has been developed. The device is designed to have a needle type sample port with a sealing cap and a cell for the reaction with the limulus reagent (stored as capsule, powder or tablet) in one compartment. The sample solution is designed to be introduced into the sealed cell compartment as jet stream through the orifice plate by reduced pressure. The device is also designed to have the parts to avoid the cross-contamination, a compartment for light-emitting diode as a light source with a light path (> 15 mm), and phototransistor for measuring optical transmittance. Single step performance of endotoxin concentration determination by simply injecting endotoxin samples (10 EU/L, 30 EU/L and 100 EU/L) to the developed device has been demonstrated.
ST development compact device measurement endotoxin concn limulus test
IT Hemocyte
(amebocyte, lysate of, limulus test; development of compact device for measuring endotoxin concentration by limulus test method)
IT Apparatus
Optical transmission
Turbidimetry
(development of compact device for measuring endotoxin concentration by limulus test method)
IT **Toxins**
RL: **ANT (Analyte)**; ANST (Analytical study)
(**endotoxins**; development of compact device for measuring **endotoxin** concentration by limulus test method)

IT **Limulus polyphemus**
(limulus test; development of compact device for measuring endotoxin concentration by limulus test method)

L16 ANSWER 8 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:238458 HCAPLUS
DN 138:298968
ED Entered STN: 28 Mar 2003
TI Endotoxin detection (LAL test)
AU Bosnic, Tamara
CS Zavod za Kontrolu Lijekova Federacije Bosne i Hercegovine, Bosnia/Herzegovina
SO Pharmacia (Sarajevo, Bosnia and Herzegovina) (2002), 13, 82-89
CODEN: PSBHAD; ISSN: 0480-2551
PB Udruzenje Farmaceuta Federacije Bosne i Hercegovine
DT Journal
LA Croatian
CC 4-1 (Toxicology)
AB The LAL (Limulus amebocyte lysate) test is the most sensitive and specific test for bacterial endotoxins using amebocyte lysate from horseshoe crab (Limulus polyphemus or Tachypleus tridentatus). Endotoxin is a very common contaminant of aqueous solution and is extremely heat-resistant. The LAL test is an alternative method to the rabbit pyrogen test. There are many advantages of the LAL test over the rabbit pyrogen test. The basis of the test is that endotoxin produces an opacity and gelation in LAL. There are 3 techniques for the LAL test: the **gel-clot** technique (gel formation), the turbidimetric technique (turbidity), and the chromogenic technique (color development, peptide-chromogen complex). The **gel-clot** LAL test method is a simple, reproducible test that is conducted by mixing equal parts of reagent and test specimen. The LAL reaction requires a neutral pH and is time- and concentration-dependent.
ST endotoxin detection Limulus amebocyte test
IT Hemocyte
(amebocyte; endotoxin detection in Limulus amebocyte test)
IT **Limulus polyphemus**
Tachypleus tridentatus
(endotoxin detection in Limulus amebocyte test)
IT **Toxins**
RL: **ANT (Analyte)**; ANST (Analytical study)
(**endotoxins; endotoxin** detection in Limulus amebocyte test)

L16 ANSWER 9 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:115765 HCAPLUS
DN 138:380535
ED Entered STN: 14 Feb 2003
TI Quantitative determination of blood endotoxin
AU Endo, Shigeatsu; Sato, Nobuhiro; Yaegaki, Yasunori; Inada, Toshiya
CS School of Medicine, Emergency Medicine, Iwate Medical University, Japan
SO Endotokishin Kenkyu (2002), 5, 31-38
CODEN: EKNEBO
PB Igaku Tosho Shuppan K.K.
DT Journal; General Review
LA Japanese
CC 4-0 (Toxicology)
Section cross-reference(s): 9, 14
AB A review on blood endotoxin determination using Limulus test kit for diagnosis of septicemia. The topics discussed are (1) principles of Limulus test and Limulus reaction cascade; (2) Limulus test kit using gelation, chromogenic substrate and turbidimetric kinetic assay; (3) specific and nonspecific reaction of Limulus test kit; (4) pos. plasma endotoxin and gram neg. septicemia; (5) endotoxemia in systemic inflammatory response syndrome (SIRS); and (6) blood endotoxin levels in septic shock, hemorrhagic shock, burn shock, liver disease, ischemia-reperfusion and acute pancreatitis.
ST review blood endotoxin Limulus test kit diagnosis septicemia
IT Bioassay

(Limulus test; blood endotoxin determination using Limulus test kit for diagnosis of septicemia)
IT Blood analysis
Diagnosis
Endotoxemia
Human
Limulus polyphemus
Test kits
(blood endotoxin determination using Limulus test kit for diagnosis of septicemia)
IT **Toxins**
RL: **ANT (Analyte)**; DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**endotoxins**; blood **endotoxin** determination using Limulus test kit for diagnosis of septicemia)
IT Inflammation
(systemic inflammatory response syndrome; blood endotoxin determination using Limulus test kit for diagnosis of septicemia)

L16 ANSWER 10 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:115761 HCAPLUS
DN 138:380534
ED Entered STN: 14 Feb 2003
TI Prospect of blood endotoxin determination by colorimetry
AU Tanaka, Shigenori
CS Central Research Lab., Seikagaku Kogyo Co., Ltd., Japan
SO Endotokishin Kenkyu (**2002**), 5, 25-30
CODEN: EKNEBO
PB Igaku Tosho Shuppan K.K.
DT Journal; General Review
LA Japanese
CC 4-0 (Toxicology)
Section cross-reference(s): 9
AB A review on determination of blood endotoxin (ET) using endotoxin-specific chromogenic Limulus test kit (Endospecy). The topics discussed are (1) endotoxin and (1→3)-β-D-glucan mediated coagulation pathway; (2) chromogenic endotoxin-specific assay using combined Limulus coagulation enzymes and their applications for clin. diagnosis; and (3) consideration for Limulus test kit.
ST review blood endotoxin colorimetry Limulus test diagnosis
IT Bioassay
(Limulus test; blood endotoxin determination using colorimetric Limulus test kit)
IT Blood analysis
Colorimetry
Diagnosis
Human
Limulus polyphemus
Test kits
(blood endotoxin determination using colorimetric Limulus test kit)
IT **Toxins**
RL: **ANT (Analyte)**; DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**endotoxins**; blood **endotoxin** determination using colorimetric Limulus test kit)

L16 ANSWER 11 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:23090 HCAPLUS
DN 138:84868
ED Entered STN: 10 Jan 2003
TI Use of recombinant horseshoe crab factor C, factor C substrate, and surfactant in endotoxin detection
IN Chen, Lin; Pepe, Michael
PA Biowhittaker, Inc., USA
SO PCT Int. Appl., 61 pp.
CODEN: PIXXD2

DT Patent
LA English
IC ICM G01N
CC 4-1 (Toxicology)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO2003002976	A2	20030109	2002WO-US20395	20020628 <--
	WO2003002976	A3	20030515		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US2003054432	A1	20030320	2002US-0183992	20020628 <--
	US---6849426	B2	20050201		
	EP---1409984	A2	20040421	2002EP-0768293	20020628 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	CN---1529711	A	20040915	2002CN-0814296	20020628 <--
	BR2002010681	A	20040921	2002BR-0010681	20020628 <--
	JP2005500520	T2	20050106	2003JP-0508913	20020628 <--
	US2004235080	A1	20041125	2004US-0480254	20040625 <--
PRAI	2001US-301125P	P	20010628 <--		
	2002WO-US20395	W	20020628 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2003002976	ICM	G01N
	IPCI	G01N [ICM,7]
	IPCR	C12Q0001-04 [I,A]; C12Q0001-04 [I,C*]; G01N0033-579 [I,A]; G01N0033-579 [I,C*]
	ECLA	C12Q001/04; G01N033/579
US2003054432	IPCI	C12Q0001-26 [ICM,7]; C12Q0001-04 [ICS,7]
	IPCR	C12Q0001-04 [I,A]; C12Q0001-04 [I,C*]; G01N0033-579 [I,A]; G01N0033-579 [I,C*]
	NCL	435/025.000; 435/034.000
	ECLA	C12Q001/04; G01N033/579
EP---1409984	IPCI	G01N0001-00 [ICM,7]
	IPCR	C12Q0001-04 [I,A]; C12Q0001-04 [I,C*]; G01N0033-579 [I,A]; G01N0033-579 [I,C*]
CN---1529711	IPCI	C07K0001-00 [ICM,7]; C07K0004-00 [ICS,7]; C07K0017-00 [ICS,7]; C12P0021-06 [ICS,7]
	IPCR	C12Q0001-04 [I,A]; C12Q0001-04 [I,C*]; G01N0033-579 [I,A]; G01N0033-579 [I,C*]
	ECLA	C12Q001/04; G01N033/579
BR2002010681	IPCI	C07K0001-00 [ICM,7]; C07K0004-00 [ICS,7]; C07K0017-00 [ICS,7]; C12P0021-06 [ICS,7]
	IPCR	C12Q0001-04 [I,A]; C12Q0001-04 [I,C*]; G01N0033-579 [I,A]; G01N0033-579 [I,C*]
JP2005500520	IPCI	G01N0033-579 [ICM,7]
	IPCR	C12Q0001-04 [I,A]; C12Q0001-04 [I,C*]; G01N0033-579 [I,A]; G01N0033-579 [I,C*]
US2004235080	IPCI	C12Q0001-37 [ICM,7]; C12Q0001-18 [ICS,7]
	IPCR	C12Q0001-04 [I,A]; C12Q0001-04 [I,C*]; G01N0033-579 [I,A]; G01N0033-579 [I,C*]
	NCL	435/023.000; 435/032.000
	ECLA	C12Q001/04; G01N033/579

OS MARPAT 138:84868
AB A reagent containing a purified horseshoe crab Factor C, particularly a recombinantly produced Factor C, and a surfactant can be used in a sensitive, rapid, and reproducible assay to detect endotoxin. Thus,

Carcinoscorpous rotundicauda factor C was prepared with recombinant baculovirus-infected Sf9 cells. Factor C activity is measured in a buffered solution containing a surfactant such as Zwittergent 3-14 and a substrate such as N-Boc-Val-Pro-Arg-7-amido-4-methylcoumarin. The presence of endotoxin increases the fluorescence. Addition of detergent increases the endotoxin detection sensitivity up to 10-fold.

ST endotoxin detn recombinant horseshoe crab factor C surfactant

IT Animal cell line
(SF9, factor C manufacture with recombinant; use of recombinant horseshoe crab factor C, factor C substrate, and surfactant in endotoxin detection)

IT Surfactants
(amphoteric; use of recombinant horseshoe crab factor C, factor C substrate, and surfactant in endotoxin detection)

IT Surfactants
(anionic; use of recombinant horseshoe crab factor C, factor C substrate, and surfactant in endotoxin detection)

IT Surfactants
(cationic; use of recombinant horseshoe crab factor C, factor C substrate, and surfactant in endotoxin detection)

IT Alcohols, analysis
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(coco, ethoxylated; use of recombinant horseshoe crab factor C, factor C substrate, and surfactant in endotoxin detection)

IT **Toxins**
RL: **ANT (Analyte)**; ANST (Analytical study)
(**endotoxins**; use of recombinant horseshoe crab factor C, factor C substrate, and surfactant in **endotoxin** detection)

IT Carcinoscorpius rotundicauda
Limulus polyphemus
Tachypleus gigas
Tachypleus tridentatus
(factor C of; use of recombinant horseshoe crab factor C, factor C substrate, and surfactant in endotoxin detection)

IT Surfactants
(nonionic; use of recombinant horseshoe crab factor C, factor C substrate, and surfactant in endotoxin detection)

IT Molecular cloning
(of horseshoe crab factor C DNA; use of recombinant horseshoe crab factor C, factor C substrate, and surfactant in endotoxin detection)

IT Surfactants
Test kits
(use of recombinant horseshoe crab factor C, factor C substrate, and surfactant in endotoxin detection)

IT 484096-53-9, 1: PN: WO03002976 SEQID: 1 unclaimed DNA 484096-55-1, 3: PN: WO03002976 SEQID: 3 unclaimed DNA 484096-57-3, 5: PN: WO03002976 SEQID: 5 unclaimed DNA 484096-59-5, 7: PN: WO03002976 SEQID: 7 unclaimed DNA
RL: PRP (Properties)
(unclaimed nucleotide sequence; use of recombinant horseshoe crab factor C, factor C substrate, and surfactant in endotoxin detection)

IT 484096-54-0 484096-56-2 484096-58-4 484096-60-8
RL: PRP (Properties)
(unclaimed protein sequence; use of recombinant horseshoe crab factor C, factor C substrate, and surfactant in endotoxin detection)

IT 65147-04-8 113866-00-5
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(use of recombinant horseshoe crab factor C, factor C substrate, and surfactant in endotoxin detection)

IT 187483-35-8P, Coagulation factor C
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(use of recombinant horseshoe crab factor C, factor C substrate, and surfactant in endotoxin detection)

IT 9002-93-1, Triton X100 9005-64-5, Tween 20 9005-65-6, Tween 80

14933-09-6, Zwittergent 3-14 85618-21-9
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(use of recombinant horseshoe crab factor C, factor C substrate, and surfactant in endotoxin detection)

L16 ANSWER 12 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:491446 HCAPLUS
DN 137:75545
ED Entered STN: 01 Jul 2002
TI Method for determining endotoxin activity with Limulus polyphemus
IN Zinkevich, O. D.; Anikhovskaya, I. A.; Safina, N. A.; Krupnik, A. N.; Salakhov, I. M.; Urazaev, R. A.; Khabriev, R. U.; Yakovlev, M. Yu.
PA ZAO "Kliniko-Diagnosticheskoe Obshchestvo", Russia
SO Russ., No pp. given
CODEN: RUXXE7
DT Patent
LA Russian
IC ICM G01N-0033/48
ICS G01N-0033/487; G01N-0033/49; G01N-0033/579
CC 9-16 (Biochemical Methods)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI RU---2169367	C1	20010620	2000RU-0121576	20000816 <--
PRAI 2000RU-0121576		20000816 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
RU 2169367	ICM	G01N-0033/48
	ICS	G01N-0033/487; G01N-0033/49; G01N-0033/579
	IPCI	G01N0033-48 [ICM,7]; G01N0033-487 [ICS,7]; G01N0033-49 [ICS,7]; G01N0033-579 [ICS,7]
	IPCR	G01N0033-48 [I,A]; G01N0033-48 [I,C*]; G01N0033-487 [I,A]; G01N0033-487 [I,C*]; G01N0033-49 [I,A]; G01N0033-49 [I,C*]; G01N0033-579 [I,A]; G01N0033-579 [I,C*]

AB The inventive method involves mixing Limulus polyphemus lysate and the diluted sample under test, with polymer causing coagulum production detected in the last dilution The polymer causing coagulum production is identified by examining protein fractals structure after drying the mixture Mixing Limulus lysate and the diluted sample under test is carried out by placing 2-8 mcl of Limulus lysate solution and the diluted sample under test onto plastic surface. The plastic surface with reagents placed thereon is covered with cover and incubated at 37 C during 30 min. It is uncovered and kept in the thermostat until reagent mixture drops dry. The polymer causing coagulum production is recognized by detecting structure of protein fractals produced. Endotoxin being available, the fractals as specific crystal-shaped structures are observed Otherwise, when no endotoxin being found or neg. control being the case, smooth field with rare intrusions of rhombic salt crystals is observed in the peripheral part of the field. The advantage is enhanced sensitivity in determining endotoxin activity.
ST endotoxin activity Limulus polymer pptn
IT **Toxins**
RL: **ANT (Analyte)**; ANST (Analytical study)
(**endotoxins**; method for determining **endotoxin** activity with Limulus polyphemus)
IT **Limulus polyphemus**
Precipitation (chemical)
(method for determining endotoxin activity with Limulus polyphemus)
IT Polymers, uses
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(method for determining endotoxin activity with Limulus polyphemus)
IT 9003-53-6, Polystyrene
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(method for determining endotoxin activity with Limulus polyphemus)

L16 ANSWER 13 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:869642 HCAPLUS
DN 136:350084
ED Entered STN: 02 Dec 2001
TI Limulus amoebocyte lysate (LAL) test - an alternative method for detection of bacterial endotoxins
AU Blechova, R.; Pivodova, D.
CS Department of Pharmacology and Toxicology, Faculty of Pharmacy, University of Veterinary and Pharmaceutical Sciences, Brno, Czech Rep.
SO Acta Veterinaria Brno (2001), 70(3), 291-296
CODEN: ACVTB9; ISSN: 0001-7213
PB University of Veterinary and Pharmaceutical Sciences
DT Journal
LA English
CC 1-1 (Pharmacology)
AB The Limulus amebocyte lysate (LAL) test is an alternative method to the rabbit pyrogen test focussed on detection of pyrogenic substances in sterile parenteral drugs. The aim of this work is the evaluation and introduction to common day use of LAL test **gel-clot** method for assay of bacterial endotoxins (the most common pyrogens) in examined product. A total number of 15 samples were tested for bacterial endotoxins to verify the method in our laboratory conditions. In 6 products, the presence of pyrogens was examined using simultaneously the LAL test and the rabbit pyrogen test. The replacement of the rabbit pyrogen test by the LAL test **gel-clot** method is possible when the endotoxin limit for the observed drug product is defined, the set maximal endotoxin concentration level in such material is acceptable and standardized test procedures and validation techniques are established. There are many advantages of LAL test over the rabbit pyrogen test, however, one of the most important aspects of LAL test is that LAL test is in accordance with the latest demand of the European Pharmacopoeia Commission for the replacement of the animal-based tests in favor of alternative methods where possible. The tests carried out have proved that the LAL test could replace the rabbit pyrogen test on condition that the validation parameters are fulfilled.
ST Limulus amoebocyte lysate test bacteria endotoxin drug; pyrogen detection Limulus amoebocyte lysate test
IT **Limulus polyphemus**
Pyrogens
(Limulus amoebocyte lysate method for detection of bacterial endotoxins in sterile parenteral drugs)
IT **Toxins**
RL: **ANT (Analyte)**; ANST (Analytical study)
(**endotoxins**; Limulus amoebocyte lysate method for detection of bacterial **endotoxins** in sterile parenteral drugs)
IT Drugs
(parental; Limulus amoebocyte lysate method for detection of bacterial endotoxins in sterile parenteral drugs)
IT Drug delivery systems
(parenterals; Limulus amoebocyte lysate method for detection of bacterial endotoxins in sterile parenteral drugs)
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) BioWhittaker Inc; Multi-test Limulus Amebocyte Lysate Pyrogentplus 1993
(2) Council of Europe; European Pharmacopoeia 3rd Edition - Supplement 2001 2000, P79
(3) Friberg, P; Detection of Bacterial Endotoxins with the Limulus Amebocyte Lysate Test 1987
(4) Levin, J; Bull Johns Hopkins Hosp 1964, P115
(5) Levin, J; Bull Johns Hopkins Hosp 1964, P337 MEDLINE
(6) Levin, J; J Lab Clin Med 1970, V75, P903 HCAPLUS
(7) Russel, W; Principles of Humane Experimental Technique 1992
(8) Young, N; J Clin Invest 1972, V51, P1790 HCAPLUS

L16 ANSWER 14 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 1999:780341 HCAPLUS

DN 132:1190
ED Entered STN: 09 Dec 1999
TI Endotoxin-specific assay
IN Loverock, Bruce
PA BioWhitaker Technologies, USA
SO U.S., 10 pp.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K-0031/715
ICS C12Q-0001/00; C12Q-0001/04
INCL 514054000
CC 4-1 (Toxicology)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US---5998389	A	19991207	1998US-0081659	19980520 <--
	JP2000002708	A2	20000107	1999JP-0139410	19990520 <--
PRAI	1998US-0081659	A	19980520 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 5998389	ICM	A61K-0031/715
	ICS	C12Q-0001/00; C12Q-0001/04
	INCL	514054000
	IPCI	A61K0031-715 [ICM,6]; C12Q0001-00 [ICS,6]; C12Q0001-04 [ICS,6]
	IPCR	G01N0033-579 [I,A]; G01N0033-579 [I,C*]
	NCL	514/054.000; 435/004.000; 435/034.000; 436/063.000; 436/074.000; 536/123.120
	ECLA	G01N033/579
JP2000002708	IPCI	G01N0033-579 [ICM,7]
	IPCR	G01N0033-579 [I,A]; G01N0033-579 [I,C*]

AB β-1,4-Glucans, particularly cellobiose, can be used to inhibit the glucan-specific enzymic pathway in an amebocyte lysate. So inhibited, the amebocyte lysate can then be used to specifically detect endotoxin in a test sample. β-1,4-glucan inhibitors can be used in a variety of amebocyte lysate assays, including kinetic-chromogenic, end-point chromogenic, turbidimetric, **gel-clot**, and ELISA assays.

ST endotoxin assay
IT Functional groups
(Carboxymethyl; endotoxin-specific assay)
IT Functional groups
(Hydroxypropyl; endotoxin-specific assay)
IT Hemocyte
(amebocyte; endotoxin-specific assay)
IT Alkyl groups
Carcinoscorpius rotundicauda
Colorimetry
Freeze drying
Hydroxyl group
Limulidae
Limulus polyphemus
Methyl group
Tachypleus gigas
Tachypleus tridentatus
Test kits
Turbidimetry
(endotoxin-specific assay)
IT **Toxins**
RL: **ANT (Analyte)**; ANST (Analytical study)
(**endotoxins; endotoxin**-specific assay)
IT Immunoassay
(enzyme-linked immunosorbent assay; endotoxin-specific assay)
IT 50-99-7, Glucose, analysis 528-50-7, Cellobiose 9051-98-3D,

β-1,4-Glucan, compds.
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(endotoxin-specific assay)
RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Anon; EP---0397880 1990 HCAPLUS
(2) Anon; EP---0330991 1994 HCAPLUS
(3) Anon; Product Brochure 1995, P1
(4) Anon; Product Brochure 1996, P1
(5) Cooper; PDA J Pharm Sci Technol 1997, V51, P2 HCAPLUS
(6) Iwanaga; Current Opinion Immunology 1993, V5, P74 HCAPLUS
(7) Kambayashi; J Biochem Biophys Methods 1991, V22, P93 HCAPLUS
(8) Matuura; US---5179006 1993 HCAPLUS
(9) Morita, T; Bacterial Endotoxins: Structure, Biomedical Signifcance, and Detection with the Limulus Amebocyte Lysate Test 1985, P53 HCAPLUS
(10) Tamura; US---5702882 1997 HCAPLUS
(11) Tanaka; US---5155032 1992 HCAPLUS
(12) Tanaka; US---5641643 1997 HCAPLUS
(13) Zhang, G; Journal of Clinical Microbiology 1994, P1537 HCAPLUS

L16 ANSWER 15 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 1999:471956 HCAPLUS
DN 131:113396
ED Entered STN: 02 Aug 1999
TI Production of Limulus lysate for determination of endotoxin
IN Tamura, Hiroshi; Tanaka, Shigenori; Akitagawa, Jun
PA Seikagaku Kogyo Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM G01N-0033/579
CC 9-2 (Biochemical Methods)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP--11201973	A2	19990730	1998JP-0002513	19980108 <--
	JP---3822974	B2	20060920		
PRAI	1998JP-0002513		19980108 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
JP 11201973	ICM	G01N-0033/579
	IPCI	G01N0033-579 [I,A]

AB Limulus amoebocyte, Limulus amoebocyte suspension, and/or C and G factor-containing solution is subjected to mech. treatment to inactivate the G factor to prepare the Limulus lysate. The Limulus lysate is useful for determination of endotoxin contamination in water and pharmaceutical with high accuracy.
ST Limulus lysate endotoxin detn
IT Hemocyte
(amebocyte, Limulus; production of Limulus lysate for determination of endotoxin)
IT Homogenization
Homogenization
(apparatus, high-speed; production of Limulus lysate for determination of endotoxin)
IT Hemolymph
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(coagulation factor G; production of Limulus lysate for determination of endotoxin)
IT Hemolymph
(coagulation factors, C; production of Limulus lysate for determination of endotoxin)
IT **Toxins**
RL: **ANT (Analyte)**; ANST (Analytical study)
(**endotoxins**; production of Limulus lysate for determination of endotoxin)

IT Mixers (processing apparatus)
Mixers (processing apparatus)
(homogenization apparatus, high-speed; production of Limulus lysate for determination of
endotoxin)
IT Limulus
(lysate; production of Limulus lysate for determination of endotoxin)
IT **Limulus polyphemus**
(production of Limulus lysate for determination of endotoxin)

L16 ANSWER 16 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 1999:271383 HCAPLUS
DN 130:307867
ED Entered STN: 03 May 1999
TI Factor G reduced amebocyte lysates for detection of bacterial endotoxins
IN Jordan, Foster T.; Chiang, Hui-Ti; Cooper, James F.; Wainwright, Norman R.
PA Charles River Laboratories, USA
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K-0014/745
ICS G01N-0033/579
CC 4-1 (Toxicology)
Section cross-reference(s): 6, 9
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO---9919355	A1	19990422	1998WO-US20823	19981002	<--
	W: AU, CA, JP					
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
	US---6270982	B1	20010807	1997US-0947584	19971009	<--
	AU---9897840	A1	19990503	1998AU-0097840	19981002	<--
	EP---1021463	A1	20000726	1998EP-0952045	19981002	<--
	EP---1021463	B1	20060301			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY					
	AT----318843	E	20060315	1998AT-0952045	19981002	<--
	US---6391570	B1	20020521	2000US-0665221	20000918	<--
	US2003104501	A1	20030605	2002US-0133212	20020426	<--
PRAI	1997US-0947584	A	19971009	<--		
	1998WO-US20823	W	19981002	<--		
	2000US-0665221	A1	20000918	<--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9919355	ICM	C07K-0014/745
	ICS	G01N-0033/579
	IPCI	C07K0014-745 [ICM,6]; C07K0014-435 [ICM,6,C*]; G01N0033-579 [ICS,6]
	IPCR	G01N0033-579 [I,A]; G01N0033-579 [I,C*]
	ECLA	G01N033/579
US---6270982	IPCI	G01N0033-554 [ICM,7]; G01N0033-53 [ICS,7]; A61K0039-02 [ICS,7]; A61K0045-00 [ICS,7]
	IPCR	G01N0033-579 [I,A]; G01N0033-579 [I,C*]
	NCL	435/007.320; 424/184.100; 424/234.100; 424/278.100; 424/282.100; 435/004.000; 435/007.200; 435/034.000; 435/184.000; 435/962.000; 514/023.000
	ECLA	G01N033/579
AU---9897840	IPCI	C07K0014-745 [ICM,6]; C07K0014-435 [ICM,6,C*]; G01N0033-579 [ICS,6]
	IPCR	G01N0033-579 [I,A]; G01N0033-579 [I,C*]
EP---1021463	IPCI	C07K0014-435 [I,C]; G01N0033-579 [I,C]; C07K0014-745 [I,A]; G01N0033-579 [I,A]
	IPCR	G01N0033-579 [I,C*]; G01N0033-579 [I,A]

	ECLA	G01N033/579
AT----318843	IPCI	C07K0014-745 [ICS,7]; C07K0014-435 [ICS,7,C*]; G01N0033-579 [ICS,7]
	IPCR	G01N0033-579 [I,C*]; G01N0033-579 [I,A]
	ECLA	G01N033/579
US---6391570	IPCI	G01N0033-554 [ICM,7]; G01N0033-53 [ICS,7]; A61K0039-02 [ICS,7]; A61K0045-00 [ICS,7]
	IPCR	G01N0033-579 [I,A]; G01N0033-579 [I,C*]
	NCL	435/007.320; 424/184.100; 424/234.100; 424/278.100; 424/282.100; 435/004.000; 435/007.200; 435/034.000; 435/184.000; 435/962.000; 514/023.000
	ECLA	G01N033/579
US2003104501	IPCI	G01N0033-554 [ICM,7]; G01N0033-569 [ICS,7]; C12P0021-06 [ICS,7]; C07K0016-12 [ICS,7]
	IPCR	G01N0033-579 [I,A]; G01N0033-579 [I,C*]
	NCL	435/007.320; 435/068.100; 530/387.100
	ECLA	G01N033/579

AB The invention provides methods and compns. for the detection and/or quantification of bacterial endotoxins. In particular, provided herein is an inexpensive and reproducible method for producing an improved amebocyte lysate preparation having reduced Factor G activity. Provided also is an endotoxin-specific amebocyte lysate preparation produced by such a method. In addition, the invention provides methods and compns. for enhancing the sensitivity to endotoxins of amebocyte lysate prepns. having reducing Factor G activity. In particular, the sensitivity of such amebocyte lysate prepns. to endotoxins can be enhanced by the addition of exogenous (1→3) β-D-glucan.

ST endotoxin bacteria analysis amebocyte lysate Factor G glucan

IT Extraction
Surfactants
(Factor G reduced amebocyte lysates for detection of bacterial endotoxins)

IT Polysaccharides, biological studies
RL: ARU (Analytical role, unclassified); BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(Factor G reduced amebocyte lysates for detection of bacterial endotoxins)

IT Sulfobetaines
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(Factor G reduced amebocyte lysates for detection of bacterial endotoxins)

IT Limulus
Limulus polyphemus
(amebocyte lysate; Factor G reduced amebocyte lysates for detection of bacterial endotoxins)

IT Hemolymph
RL: ARU (Analytical role, unclassified); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PUR (Purification or recovery); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process)
(coagulation factor G; Factor G reduced amebocyte lysates for detection of bacterial endotoxins)

IT Bacteria (Eubacteria)
(endotoxin; Factor G reduced amebocyte lysates for detection of bacterial endotoxins)

IT **Toxins**
RL: **ANT (Analyte)**; BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(**endotoxins**, bacterial; Factor G reduced amebocyte lysates for detection of bacterial **endotoxins**)

IT Cotton
(extract; Factor G reduced amebocyte lysates for detection of bacterial endotoxins)

IT Surfactants
(zwitterionic; Factor G reduced amebocyte lysates for detection of bacterial endotoxins)
IT 9004-35-7, Cellulose acetate 9008-22-4, Laminaran 9037-88-1, Pachyman 9050-67-3, Schizophyllan 9051-97-2, (1,3)-.β.-Glucan 37339-90-5, Lentinan 54328-34-6, Coriolan 54724-00-4, Curdlan
RL: ARU (Analytical role, unclassified); BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(Factor G reduced amebocyte lysates for detection of bacterial endotoxins)
IT 67-66-3, Chloroform, biological studies 2281-11-0, Zwittergent 3-16 14933-08-5, Zwittergent 3-12 14933-09-6, Zwittergent 3-14 15163-36-7, Zwittergent 3-10 15178-76-4
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(Factor G reduced amebocyte lysates for detection of bacterial endotoxins)
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Mallinckrodt Inc; GB---2080524 A 1982 HCAPLUS
(2) Roslansky; DATABASE MEDLINE ABSTRACT 92129515
(3) Roslansky; JOURNAL OF CLINICAL MICROBIOLOGY 1991, V29(11), P2477 HCAPLUS
(4) Shigenori, T; US---5155032 A 1992 HCAPLUS
(5) Shigenori, T; US---5401647 A 1995 HCAPLUS
(6) Shigenori, T; US---5605806 A 1997 HCAPLUS

L16 ANSWER 17 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 1998:712199 HCAPLUS
DN 130:29322
ED Entered STN: 10 Nov 1998
TI Measuring method for endotoxin in phospholipids.
IN Kaneda, Yoshihiro; Kishimoto, Yoko; Saito, Koichi; Tokuyama, Satoru
PA Nippon Oil and Fats Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM G01N-0033/579
ICS A61K-0009/127
CC 64-1 (Pharmaceutical Analysis)
Section cross-reference(s): 4
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP--10293129	A2	19981104	1997JP-0101197	19970418 <--
PRAI	1997JP-0101197		19970418 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
JP 10293129	ICM	G01N-0033/579
	ICS	A61K-0009/127
	IPCI	G01N0033-579 [ICM,6]; A61K0009-127 [ICS,6]
	IPCR	A61K0009-127 [N,A]; A61K0009-127 [N,C*]; G01N0033-579 [I,A]; G01N0033-579 [I,C*]

AB An accurate method is described for measuring endotoxin contained in phospholipids. Phospholipid is removed by centrifugation after being emulsified or suspended in water containing anionic macromol. metal salt (e.g. polyacrylic acid sodium salt) and alkali metal salt (e.g. sodium chloride). Endotoxin in the remaining water is determined by synthetic substrate method using Limulus amebocyte lysate (LAL) component.
ST endotoxin assay phospholipid emulsification suspension; Limulus amebocyte lysate test endotoxin
IT **Toxins**
RL: **ANT (Analyte)**; ANST (Analytical study)
(**endotoxins**; measuring method for **endotoxin** in

phospholipids)
IT Drug delivery systems
(liposomes; measuring method for endotoxin in phospholipids)
IT Colorimetry
Emulsification
Limulus polyphemus
Suspensions
(measuring method for endotoxin in phospholipids)
IT Phospholipids, analysis
RL: AMX (Analytical matrix); ANST (Analytical study)
(measuring method for endotoxin in phospholipids)
IT 2644-64-6, Dipalmitoylphosphatidylcholine 4539-70-2, Distearoylphosphatidylcholine 18656-38-7, Dimyristoylphosphatidylcholine
RL: AMX (Analytical matrix); ANST (Analytical study)
(measuring method for endotoxin in phospholipids)
IT 7647-14-5, Sodium chloride, analysis 9003-04-7, Polyacrylic acid sodium salt
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(measuring method for endotoxin in phospholipids)

L16 ANSWER 18 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 1996:206094 HCAPLUS
DN 124:309621
ED Entered STN: 11 Apr 1996
TI Limulus amebocyte lysate (LAL) assays
AU **Novitsky, Thomas J.**
CS Associates **Cape Cod**, Inc., USA
SO Automated Microbial Identification and Quantitation (1996), 277-98.
Editor(s): Olson, Wayne P. Publisher: Interpharm Press, Buffalo Grove, Ill.
CODEN: 62NTA8
DT Conference; General Review
LA English
CC 4-0 (Toxicology)
Section cross-reference(s): 9, 64
AB A review with many refs. about the LAL bioassay for the detection of pyrogens (endotoxins) in applications such as end product testing, in-process control, clin. diagnosis, food anal., environmental anal., with information on the nature of the test, sensitivity, reagents, stds., FDA guidelines, etc.
ST review Limulus amebocyte lysate bioassay endotoxin
IT Bioassay
(Limulus amebocyte lysate assays for endotoxins)
IT **Limulus polyphemus**
(amebocyte lysate; Limulus amebocyte lysate assays for endotoxins)
IT Pyrogens
(bacterial, Limulus amebocyte lysate assays for endotoxins)
IT Lipopolysaccharides
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(bacterial, Limulus amebocyte lysate assays for endotoxins)
IT **Toxins**
RL: **ANT (Analyte)**; THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(endo-, Limulus amebocyte lysate assays for **endotoxins**)

L16 ANSWER 19 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 1994:624181 HCAPLUS
DN 121:224181
ED Entered STN: 12 Nov 1994
TI Reagent, kit, and method for endotoxin assay using a limulus amebocyte lysate reagent and aprotinin as factor G activation inhibitor
IN Tanaka, Shigenori; Tamura, Hiroshi; Aita, Kazuhiro
PA Seikagaku Kogyo K. K., Japan
SO Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW

DT Patent
LA English
IC ICM G01N-0033/579
CC 4-1 (Toxicology)
Section cross-reference(s): 7, 9

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP----613004	A1	19940831	1994EP-0102889	19940225 <--
	EP----613004	B1	19981223		
	R: DE, DK, FR, GB, IT, SE				
	JP--06258326	A2	19940916	1993JP-0061464	19930226 <--
	JP---3242733	B2	20011225		
	CA---2116315	AA	19940827	1994CA-2116315	19940223 <--
	AU---9456406	A1	19940901	1994AU-0056406	19940225 <--
	AU----666605	B2	19960215		
	CN---1105757	A	19950726	1994CN-0103286	19940226 <--
	US---5695948	A	19971209	1996US-0661705	19960611 <--
	US---5840510	A	19981124	1997US-0885176	19970630 <--
PRAI	1993JP-0061464	A	19930226	<--	
	1994US-0202177	B1	19940225	<--	
	1996US-0661705	A3	19960611	<--	

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
EP 613004	ICM	G01N-0033/579
	IPCI	G01N0033-579 [ICM,5]
	IPCR	G01N0033-579 [I,A]; G01N0033-579 [I,C*]
	ECLA	G01N033/579
JP--06258326	IPCI	G01N0033-579 [ICM,5]; G01N0033-543 [ICS,5]
CA---2116315	IPCI	G01N0033-579 [ICM,5]; C12Q0001-37 [ICS,5]
	IPCR	G01N0033-579 [I,A]; G01N0033-579 [I,C*]
AU---9456406	IPCI	G01N0033-68 [ICM,5]; G01N0033-579 [ICS,5]; G01N0033-543 [ICS,5]
	IPCR	G01N0033-579 [I,A]; G01N0033-579 [I,C*]
CN---1105757	IPCI	G01N0033-50 [ICM,5]; G01N0033-579 [ICS,5]
	IPCR	G01N0033-579 [I,A]; G01N0033-579 [I,C*]
US---5695948	IPCI	C12Q0001-56; C12Q0001-00; C12Q0001-34; C12Q0001-44
	IPCR	G01N0033-579 [I,A]; G01N0033-579 [I,C*]
	NCL	435/013.000; 435/004.000; 435/007.900; 435/018.000; 435/019.000; 435/023.000; 435/024.000; 435/029.000
	ECLA	G01N033/579
US---5840510	IPCI	C12Q0001-37; C12Q0001-56; C12Q0001-00; C12Q0001-34
	IPCR	G01N0033-579 [I,A]; G01N0033-579 [I,C*]
	NCL	435/018.000; 252/374.000; 424/094.100; 424/094.600; 435/004.000; 435/967.000; 436/074.000; 436/079.000; 544/358.000
	ECLA	G01N033/579

AB This invention provides (1) a reagent for endotoxin assay which comprises aprotinin and a limulus amebocyte lysate reagent, (2) a kit for endotoxin assay which comprises the limulus amebocyte lysate reagent and a reagent containing aprotinin, (3) a method for assaying endotoxin in a sample using the limulus amebocyte lysate reagent in which aprotinin is added to the lysate reagent and/or the sample, (4) a method for assaying endotoxin in a serine protease-containing sample using the limulus amebocyte lysate reagent in which the sample is allowed to contact with an aprotinin-immobilized insol. carrier in advance of endotoxin assay, (5) a carrier for pretreating a serine protease-containing sample on which aprotinin is immobilized, (6) a method for inhibiting factor G activation in which aprotinin is added to the limulus amebocyte lysate reagent and (7) a factor G activation inhibitor which comprises aprotinin as an active ingredient. The endotoxin assay can be effected based on the factor C system reaction, without influences of factor G contained in the limulus amebocyte lysate reagent and/or serine proteases contained in samples. Endotoxin was determined using a reagent containing Tachypleus tridentatus lysate reagent, Boc-Leu-Gly-Arg-pNA, and aprotinin; β-glucan had no

influence on the assay.
ST endotoxin limulus amebocyte lysate assay aprotinin; serine protease endotoxin assay aprotinin; glucan beta endotoxin assay aprotinin
IT Blood analysis
(anal. matrix; reagent, kit, and method for endotoxin assay using a limulus amebocyte lysate reagent and aprotinin as factor G activation inhibitor)
IT Limulus
Limulus polyphemus
Sepsis and Septicemia
Tachypleus tridentatus
(reagent, kit, and method for endotoxin assay using a limulus amebocyte lysate reagent and aprotinin as factor G activation inhibitor)
IT **Toxins**
RL: **ANT (Analyte)**; ANST (Analytical study)
(endo-, reagent, kit, and method for **endotoxin** assay using a limulus amebocyte lysate reagent and aprotinin as factor G activation inhibitor)
IT 9002-04-4, Thrombin 9002-07-7, Trypsin 9051-97-2, (1→3)β-D-Glucan 37259-58-8, Serine protease 153423-59-7
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(endotoxin assay inhibitor; reagent, kit, and method for endotoxin assay using a limulus amebocyte lysate reagent and aprotinin as factor G activation inhibitor)
IT 9087-70-1, Aprotinin 9087-70-1D, Aprotinin, immobilized 107527-90-2D, Formyl-cellulofine, aprotinin conjugates
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(reagent, kit, and method for endotoxin assay using a limulus amebocyte lysate reagent and aprotinin as factor G activation inhibitor)

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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 20 September 2006 (20060920/ED)

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L28 ANSWER 1 OF 14 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN 2000:540510 BIOSIS
DN PREV200000540510
TI Use of rENP to quantitate **endotoxin** by fluorescence polarization.
AU Sloyer, Jack [Reprint author]; **Novitsky, Tom** [Reprint author]
CS Associates of Cape Cod, Inc., Falmouth, MA, 02540, USA
SO Journal of Endotoxin Research, (2000) Vol. 6, No. 2, pp. 101. print.
Meeting Info.: 6th Conference of the International Endotoxin Society. Paris, France. August 24-27, 2000.
ISSN: 0968-0519.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 13 Dec 2000
Last Updated on STN: 11 Jan 2002
CC Toxicology - General and methods 22501
General biology - Symposia, transactions and proceedings 00520
IT Major Concepts
Methods and Techniques; Toxicology
IT Chemicals & Biochemicals

endotoxin; recombinant **endotoxin** neutralizing protein
IT Methods & Equipment
HPLC [high performance liquid chromatography]: purification method;
LAL-gel clot: analytical method;
fluorescence polarization: analytical method
IT Miscellaneous Descriptors
Meeting Abstract

L28 ANSWER 2 OF 14 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN **2000:386838** BIOSIS
DN PREV200000386838
TI Reversible binding of heparin to the loop peptide of **endotoxin** neutralizing protein.
AU **Ridge, Richard J.**; Paus, Erik J.; **Novitsky, Thomas J.**; Ketchum, Paul A. [Reprint author]
CS Associates of Cape Cod, Inc., 704 Main Street, Falmouth, MA, 02540, USA
SO Journal of Endotoxin Research, (**2000**) Vol. 6, No. 1, pp. 17-23. print.
ISSN: 0968-0519.
DT Article
LA English
ED Entered STN: 13 Sep 2000
Last Updated on STN: 8 Jan 2002
AB **Endotoxin** neutralizing protein (ENP) from **Limulus** polyphemus is an amphipathic, 11.8 kDa protein with an isoelectric point of 10.2. ENP neutralizes lipopolysaccharide (LPS) and possesses antibacterial activity against Gram-negative bacteria. Heparin binds to ENP and blocks its LPS-neutralizing activity. The relative blocking activity of heparin is equal to low molecular weight heparin and polyanetholsulfonic acid > heparan sulfate > chondroitin sulfate A > chondroitin sulfate C. Endoproteinase Glu-C hydrolysis of recombinant ENP results in four major peptides, three of which are seen following separation on reversed phase HPLC. Heparin binds to the loop peptide (31-72), which includes the heparin binding consensus sequence XBBXBX between the two cysteine residues of ENP. When heparin is added to the digest and then applied to a C18 column, the loop peptide is bound; however, it dissociates and elutes with either 5 M NaCl or 0.1 M sodium phosphate, demonstrating reversible binding to heparin. LPS and lipid A both bind to the loop peptide and remove it from digests of ENP; however, neither complex could be dissociated by salt or sodium phosphate. Heparin, LPS, and lipid A individually bind to the same site on ENP.
CC Physiology and biochemistry of bacteria 31000
Biochemistry studies - General 10060
Biochemistry studies - Lipids 10066
Biochemistry studies - Carbohydrates 10068
Invertebrata: comparative, experimental morphology, physiology and pathology - Arthropoda: chelicerata 64060
IT Major Concepts
Biochemistry and Molecular Biophysics
IT Chemicals & Biochemicals
endotoxin neutralizing protein: loop peptide; heparin: reversible binding; lipid A; lipopolysaccharide
ORGN Classifier
Bacteria 05000
Super Taxa
Microorganisms
Organism Name
gram-negative bacteria: pathogen
Taxa Notes
Bacteria, Eubacteria, Microorganisms
ORGN Classifier
Merostomata 75404
Super Taxa
Chelicerata; Arthropoda; Invertebrata; Animalia
Organism Name

Limulus polyphemus
Taxa Notes
Animals, Arthropods, Chelicerates, Invertebrates
RN 9005-49-6 (heparin)

L28 ANSWER 3 OF 14 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN **1998:484605** BIOSIS
DN PREV199800484605
TI **Limulus amebocyte** lysate assay for detection of **endotoxin** in patients with sepsis syndrome.
AU Bates, David W. [Reprint author]; Parsonnet, Jeffrey; Ketchum, Paul A.; Miller, Elizabeth B.; **Novitsky, Thomas J.**; Sands, Kenneth; Hibberd, Patricia L.; Graman, Paul S.; Lanken, Paul N.; Schwartz, J. Sanford; Kahn, Katherine; Snydman, David R.; Moore, Richard; Black, Edgar; Platt, Richard
CS Div. Gen. Med., Dep. Med., Brigham and Women's Hosp., 75 Francis St., Boston, MA 02115, USA
SO Clinical Infectious Diseases, (**Sept., 1998**) Vol. 27, No. 3, pp. 582-591. print.
CODEN: CIDIEL. ISSN: 1058-4838.
DT Article
LA English
ED Entered STN: 5 Nov 1998
Last Updated on STN: 5 Nov 1998
AB Clinical predictions alone are insufficiently accurate to identify patients with specific types of bloodstream infection; laboratory assays might improve such predictions. Therefore, we performed a prospective cohort study of 356 episodes of sepsis syndrome and did **Limulus amebocyte** lysate (**LAL**) assays for **endotoxin**. The main outcome measures were bacteremia and infection due to gram-negative organisms; other types of infection were secondary outcomes. Assays were defined as positive if the result was gtoreq0.4 enzyme-linked immunosorbent assay units per milliliter. There were positive assays in 119 (33%) of 356 episodes. Assay positivity correlated with the presence of fungal bloodstream infection ($P < .003$) but correlated negatively with the presence of gram-negative organisms in the bloodstream ($P = .04$). A trend toward higher rates of mortality in the **LAL** assay positive episodes was no longer present after adjusting for severity. Thus, results of **LAL** assay did not correlate with the presence of bacteremia due to gram-negative organisms or with mortality after adjusting for severity but did correlate with the presence of fungal bloodstream infection.
CC Pathology - Diagnostic 12504
Pathology - Therapy 12512
Medical and clinical microbiology - General and methods 36001
IT Major Concepts
Infection; Methods and Techniques
IT Diseases
sepsis syndrome: bacterial disease, fungal disease, infectious disease
Sepsis Syndrome (MeSH)
IT Chemicals & Biochemicals
endotoxin
IT Methods & Equipment
limulus amebocyte lysate assay: diagnostic method
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human: adult, male, female, middle age, patient
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

L28 ANSWER 4 OF 14 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN **1997:269187** BIOSIS
DN PREV199799560905

TI Utilization of a chromogenic **Limulus amebocyte** lysate blood assay in a multi-center study of sepsis.
AU Ketchum, P. A. [Reprint author]; Parsonnet, J.; Stotts, L. S.; **Novitsky, T. J.**; Schlain, B.; Bates, D. W.; Project, Investigators Of The Amcc Sepsis
CS Associates Cape Cod Inc., PO Box 224, Woods Hole, MA 02543-0224, USA
SO Journal of Endotoxin Research, (**1997**) Vol. 4, No. 1, pp. 9-16. ISSN: 0968-0519.
DT Article
LA English
ED Entered STN: 24 Jun 1997
Last Updated on STN: 24 Jun 1997
AB We conducted a prospective study of a chromogenic **LAL** assay in 346 patients with sepsis syndrome, as defined by a modification of the Bone criteria, and 131 healthy volunteers at eight member centers of the Academic Medical College Consortium (AMCC). We identified patients with endotoxemia (gt 0.40 EU/ml) by measuring **LAL**-reactive material in whole blood, extracted by the Tamura nitric acid method, with the chromogenic **LAL** (Pyrochrome) assay. The mean result in sepsis patients with detectable endotoxemia (n = 241) was 1.07 +- 1.57 EU/ml, and the mean result in 131 volunteers was 0. 1 51 +- 0.113 EU/ml, with 73% of the volunteers' results falling below the detectable limit. The average incidence of endotoxemia in sepsis patients was 33%, but varied 2.7-fold among the clinical centers (range 16-44%). Assay results were repeatable when samples tested frozen at the clinical sites were compared to results on frozen samples tested at Associates of Cape Cod, Inc. (ACC). Multiple samples were obtained from 40 patients at 18-24 h interval(s). Fourteen multidraw patients (35%) were endotoxemic at one or more draw(s) and eight of these patients had two or more draws with **endotoxin** levels gt 1.0 EU/ml. The presence of sulfa drugs gave false positive results in two patient samples. A positive **LAL** test did not correlate with culture-proven bacterial infection and did not significantly correlate with mortality. There was a correlation (P= 0.014) between a patient having a positive **LAL** test and the presence of a fungal infection when mixed fungal and bacterial infections were included. There was no correlation with a positive **LAL** test when only a fungal infection was present (P = 0.425) or when only a fungal and a Gram-positive infection was present (P = 0.087).
CC Blood - General and methods 15001
Toxicology - General and methods 22501
Medical and clinical microbiology - General and methods 36001
IT Major Concepts
Blood and Lymphatics (Transport and Circulation); Infection; Toxicology
IT Miscellaneous Descriptors
BACTERIAL DISEASE; BLOOD AND LYMPHATICS; CHROMOGENIC **LIMULUS AMEBOCYTE** LYSATE BLOOD ASSAY; DIAGNOSTIC METHOD; ENDOTOXEMIA; FUNGAL DISEASE; FUNGAL INFECTION; INFECTION; MULTI-CENTER STUDY; PATHOGEN; PATIENT; SEPSIS SYNDROME; SEROLOGY; WHOLE BLOOD
ORGN Classifier
Enterobacteriaceae 06702
Super Taxa
Facultatively Anaerobic Gram-Negative Rods; Eubacteria; Bacteria; Microorganisms
Organism Name
Enterobacter
Taxa Notes
Bacteria, Eubacteria, Microorganisms
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

L28 ANSWER 5 OF 14 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN **1995:290959** BIOSIS
DN PREV199598305259
TI Multicenter study of endotoxemia in sepsis patients using the **LAL** assay for **endotoxin.**
AU Ketchum, P. A. [Reprint author]; Stotts, L. S.; **Novitsky, T. J.**; Parsonnet, J.; Investigators, The Academic Medical Center Consortium Sepsis
CS Associates Cape Cod Inc., Woods Hyole, MA, USA
SO Abstracts of the General Meeting of the American Society for Microbiology, (1995) Vol. 95, No. 0, pp. 287.
Meeting Info.: 95th General Meeting of the American Society for Microbiology. Washington, D.C., USA. May 21-25, 1995.
ISSN: 1060-2011.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 5 Jul 1995
Last Updated on STN: 5 Jul 1995
CC General biology - Symposia, transactions and proceedings 00520
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Carbohydrates 10068
Toxicology - General and methods 22501
Physiology and biochemistry of bacteria 31000
Microbiological apparatus, methods and media 32000
Immunology - Bacterial, viral and fungal 34504
Immunology - Immunopathology, tissue immunology 34508
Medical and clinical microbiology - Bacteriology 36002
IT Major Concepts
Clinical Endocrinology (Human Medicine, Medical Sciences); Immune System (Chemical Coordination and Homeostasis); Infection
IT Miscellaneous Descriptors
LIMULUS AMOEBOCYTE LYSATE ASSAY; MEETING ABSTRACT
ORGN Classifier
Bacteria 05000
Super Taxa
Microorganisms
Organism Name
bacteria
Taxa Notes
Bacteria, Eubacteria, Microorganisms
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

L28 ANSWER 6 OF 14 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN **1992:28821** BIOSIS
DN PREV199293018096; BA93:18096
TI SENSITIVITY OF **LIMULUS AMOEBOCYTE** LYSATE **LAL** TO **LAL**-REACTIVE GLUCANS.
AU ROSLANSKY P F [Reprint author]; **NOVITSKY T J**
CS ASSOCIATES CAPE COD INC, BOX 224, WOODS HOLE, MASS 02543, USA
SO Journal of Clinical Microbiology, (1991) Vol. 29, No. 11, pp. 2477-2483.
CODEN: JCMIDW. ISSN: 0095-1137.
DT Article
FS BA
LA ENGLISH
ED Entered STN: 6 Jan 1992
Last Updated on STN: 6 Mar 1992
AB The sensitivity of **Limulus amebocyte** lysate (

LAL)-reactive glucans (LRGs) and lipid A was tested by using commercially available and experimentally formulated **LAL** reagents. The glucans included two kinds of β-(1,3)-D-glucans, laminarin and curdlan, and cellulosic material, **LAL**-reactive material (**LAL**-RM), extracted from a hollow-fiber (Cuprophan) hemodialyzer. **LAL**-RM loses its **LAL** activity when it is digested with cellulase and thus appears to be β(1,4)-D-glucan or a mixed glucan containing a substantial proportion of β-(1,4) linkages. All **LAL** reagents tested were at least 1,000-fold more sensitive to **endotoxin** than to LRGs. The presence of the surfactant Zwittergent was shown to interfere with reactivity to LRGs, **LAL** reagents without added Zwittergent reacted more strongly to LRGs than did the same reagents containing Zwittergent. Chloroform extraction of **LAL** increased the reagents' sensitivity to both **endotoxin** and LRGs, but it was not responsible for LRG reactivity. The addition of Zwittergent significantly reduced the sensitivity of **LAL** reagents to lipid A. **LAL** without the surfactant was equally sensitive to **endotoxin** and lipid A. Both curdlan and **LAL**-RM amplified or enhanced the **LAL** response to **endotoxin.** Kinetic turbidimetric studies demonstrated that the enhancement was dependent on the glucan concentration.

CC Biochemistry methods - Lipids 10056
Biochemistry methods - Carbohydrates 10058
Biochemistry studies - Lipids 10066
Biochemistry studies - Carbohydrates 10068
Toxicology - General and methods 22501
Physiology and biochemistry of bacteria 31000
Microbiological apparatus, methods and media 32000
Medical and clinical microbiology - General and methods 36001
Medical and clinical microbiology - Bacteriology 36002
Invertebrata: comparative, experimental morphology, physiology and pathology - Arthropoda: chelicerata 64060

IT Major Concepts
Biochemistry and Molecular Biophysics; Infection; Methods and Techniques; Toxicology

IT Miscellaneous Descriptors
ENDOTOXIN DETECTION METHOD LAMINARIN CURDLAN HEMODIALYSIS FILTER EXTRACT ZWITTERGENT SURFACTANT LIPID A **AMOEBOCYTE**

ORGN Classifier
Bacteria 05000
Super Taxa
Microorganisms
Taxa Notes
Bacteria, Eubacteria, Microorganisms

RN 9012-72-0D (GLUCANS)
9008-22-4 (LAMINARIN)
54724-00-4 (CURDLAN)
71833-44-8 (ZWITTERGENT)
9037-91-6DQ (GLUCANS)
95991-05-2 (LIPID A)

L28 ANSWER 7 OF 14 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN **1991:273337** BIOSIS
DN PREV199192005952; BA92:5952
TI PLASTICS **ENDOTOXINS** AND THE **LIMULUS AMEBOCYTE** LYSATE TEST.
AU ROSLANSKY P F [Reprint author]; DAWSON M E; **NOVITSKY T J**
CS PO BOX 224, WOODS HOLE, MASS 02543, USA
SO Journal of Parenteral Science and Technology, (**1991**) Vol. 45, No. 2, pp. 83-87.
CODEN: JPATDS. ISSN: 0279-7976.
DT Article
FS BA
LA ENGLISH
ED Entered STN: 13 Jun 1991
Last Updated on STN: 14 Jun 1991

AB A variety of polypropylene and polystyrene tubes have been tested for use with the **Limulus amebocyte** lysate (**LAL**) test. Polypropylene tubes tended to be more contaminated with **endotoxin** than polystyrene. One brand of polypropylene tube contained a water extractable inhibitor of **LAL** test. Polystyrene tube from some manufactures caused enhancement of the **LAL** test. Other polystyrene tubes were not significantly different from glass for storage of **endotoxin** or dilution water. Results of these studies indicate than while some tubes are well suited for use with the **LAL** test, others are not.
CC Biochemistry studies - Lipids 10066
Biochemistry studies - Carbohydrates 10068
Pathology - Diagnostic 12504
Toxicology - General and methods 22501
Physiology and biochemistry of bacteria 31000
Microbiological apparatus, methods and media 32000
Medical and clinical microbiology - Bacteriology 36002
IT Major Concepts
Infection; Methods and Techniques; Pathology; Physiology; Toxicology
IT Miscellaneous Descriptors
POLYPROPYLENE POLYSTYRENE DIAGNOSIS
ORGN Classifier
Bacteria 05000
Super Taxa
Microorganisms
Taxa Notes
Bacteria, Eubacteria, Microorganisms
ORGN Classifier
Merostomata 75404
Super Taxa
Chelicerata; Arthropoda; Invertebrata; Animalia
Taxa Notes
Animals, Arthropods, Chelicerates, Invertebrates
RN 9003-07-0 (POLYPROPYLENE)
9003-53-6 (POLYSTYRENE)

L28 ANSWER 8 OF 14 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN **1989:291054** BIOSIS
DN PREV198988016398; BA88:16398
TI SINGLE-STEP CHROMOGENIC **LIMULUS AMEBOCYTE** LYSATE ASSAY FOR **ENDOTOXIN.**
AU LINDSAY G K [Reprint author]; ROSLANSKY P F; **NOVITSKY T J**
CS ASSOCIATED CAPE COD, INC, FALMOUTH, MASS 02540, USA
SO Journal of Clinical Microbiology, (**1989**) Vol. 27, No. 5, pp. 947-951.
CODEN: JCMIDW. ISSN: 0095-1137.
DT Article
FS BA
LA ENGLISH
ED Entered STN: 20 Jun 1989
Last Updated on STN: 20 Jun 1989
AB A new reagent for the chromogenic **Limulus amebocyte** lysate (**LAL**) assay is described. **LAL** was formulated for optimal performance in either an endpoint procedure or a kinetic procedure with the chromogenic substrate, buffer, and **LAL** components colyophilized as a single reagent. The kinetic chromogenic method required an incubating microplate reader coupled to a computer for collection and analysis of data. The kinetic method had a longer incubation time than the endpoint method and spanned a range of over 3 orders of magnitude compared with the 1-order-of-magnitude range of the endpoint assay. The kinetic method was less subject to operator error, since readings were continuous and automatic. The endpoint test was more operator intensive, requiring both addition of acetic acid to stop the reaction and transfer of the sample to the reading device. A single-step chromogenic reagent was also prepared without lyophilization by mixing reconstituted **gel clot LAL** with a buffer and

a chromogenic substrate. The reagent prepared in this manner performed as well as the colyophilized agent.
CC Biochemistry methods - General 10050
Biochemistry methods - Lipids 10056
Biochemistry methods - Carbohydrates 10058
Biophysics - Bioengineering 10511
Enzymes - Methods 10804
Pathology - Diagnostic 12504
Toxicology - General and methods 22501
Physiology and biochemistry of bacteria 31000
Microbiological apparatus, methods and media 32000
Medical and clinical microbiology - General and methods 36001
Medical and clinical microbiology - Bacteriology 36002
Invertebrata: comparative, experimental morphology, physiology and pathology - Arthropoda: chelicerata 64060
IT Major Concepts
Infection; Methods and Techniques; Toxicology
IT Miscellaneous Descriptors
ENDPOINT VS. KINETIC PROCEDURE AUTOMATION
ORGN Classifier
Bacteria 05000
Super Taxa
Microorganisms
Taxa Notes
Bacteria, Eubacteria, Microorganisms
ORGN Classifier
Merostomata 75404
Super Taxa
Chelicerata; Arthropoda; Invertebrata; Animalia
Taxa Notes
Animals, Arthropods, Chelicerates, Invertebrates

L28 ANSWER 9 OF 14 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN **1987:411410** BIOSIS
DN PREV198733081088; BR33:81088
TI QUANTITATION OF **ENDOTOXIN** IN PRODUCTS USING THE **LAL** KINETIC TURBIDIMETRIC ASSAY.
AU REMILLARD J F [Reprint author]; GOULD M C; ROSLANSKY P F; **NOVITSKY T J**
CS ASSOCIATES OF CAPE COD INC, WOODS HOLE, MASS 02543, USA
SO Prog. Clin. Biol. Res., (**1987**) pp. 197-210. WATSON, S. W., J. LEVIN AND T. J. NOVITSKY (ED.). PROGRESS IN CLINICAL AND BIOLOGICAL RESEARCH, VOL. 231. DETECTION OF BACTERIAL ENDOTOXINS WITH LIMULUS AMEBOCYTE LYSATE TEST; INTERNATIONAL CONFERENCE, WOODS HOLE, MASSACHUSETTS, USA, SEPTEMBER 8-11, 1985. XIX+528P. ALAN R. LISS, INC.: NEW YORK, NEW YORK, USA. ILLUS.
Publisher: Series: Progress in Clinical and Biological Research.
CODEN: PCBRD2. ISSN: 0361-7742. ISBN: 0-8451-5081-2.
DT Book
Conference; (Meeting)
FS BR
LA ENGLISH
ED Entered STN: 27 Sep 1987
Last Updated on STN: 27 Sep 1987
CC General biology - Symposia, transactions and proceedings 00520
Comparative biochemistry 10010
Biochemistry methods - General 10050
Biochemistry studies - General 10060
Biochemistry studies - Lipids 10066
Biochemistry studies - Carbohydrates 10068
Pharmacology - General 22002
Toxicology - General and methods 22501
Physiology and biochemistry of bacteria 31000
Microbiological apparatus, methods and media 32000
Medical and clinical microbiology - General and methods 36001
Medical and clinical microbiology - Bacteriology 36002

IT Major Concepts
Biochemistry and Molecular Biophysics; Infection; Physiology; Toxicology
IT Miscellaneous Descriptors
BACTERIA **LIMULUS AMOEBOCYTE** LYSATE METHODS DRUGS
ORGN Classifier
Bacteria 05000
Super Taxa
Microorganisms
Taxa Notes
Bacteria, Eubacteria, Microorganisms

L28 ANSWER 10 OF 14 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN **1987:411409** BIOSIS
DN PREV198733081087; BR33:81087
TI DESIGN CRITERIA AND EVALUATION OF THE **LAL**-4000 FOR KINETIC TURBIDIMETRIC **LAL** ASSAY.
AU **NOVITSKY T J** [Reprint author]; REMILLARD J F; LOY N
CS ASSOCIATE OF CAPE COD INC, WOODS HOLE, MA 02543, USA
SO Prog. Clin. Biol. Res., (**1987**) pp. 189-196. WATSON, S. W., J. LEVIN AND T. J. NOVITSKY (ED.). PROGRESS IN CLINICAL AND BIOLOGICAL RESEARCH, VOL. 231. DETECTION OF BACTERIAL ENDOTOXINS WITH LIMULUS AMEBOCYTE LYSATE TEST; INTERNATIONAL CONFERENCE, WOODS HOLE, MASSACHUSETTS, USA, SEPTEMBER 8-11, 1985. XIX+528P. ALAN R. LISS, INC.: NEW YORK, NEW YORK, USA. ILLUS.
Publisher: Series: Progress in Clinical and Biological Research.
CODEN: PCBRD2. ISSN: 0361-7742. ISBN: 0-8451-5081-2.
DT Book
Conference; (Meeting)
FS BR
LA ENGLISH
ED Entered STN: 27 Sep 1987
Last Updated on STN: 27 Sep 1987
CC General biology - Symposia, transactions and proceedings 00520
General biology - Information, documentation, retrieval and computer applications 00530
Methods - Laboratory methods 01004
Mathematical biology and statistical methods 04500
Biochemistry methods - General 10050
Biochemistry studies - General 10060
Biochemistry studies - Lipids 10066
Biochemistry studies - Carbohydrates 10068
Toxicology - General and methods 22501
Physiology and biochemistry of bacteria 31000
Microbiological apparatus, methods and media 32000
Medical and clinical microbiology - General and methods 36001
Medical and clinical microbiology - Bacteriology 36002
IT Major Concepts
Biochemistry and Molecular Biophysics; Infection; Physiology; Toxicology
IT Miscellaneous Descriptors
BACTERIAL **ENDOTOXINS LIMULUS AMOEBOCYTE** LYSATE COMPUTER STATISTICAL METHODS
ORGN Classifier
Bacteria 05000
Super Taxa
Microorganisms
Taxa Notes
Bacteria, Eubacteria, Microorganisms

L28 ANSWER 11 OF 14 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN **1987:411396** BIOSIS
DN PREV198733081074; BR33:81074
TI PROGRESS IN CLINICAL AND BIOLOGICAL RES. VOL. 231 DETECTION OF BACTERIAL

ENDOTOXINS WITH LIMULUS AMOEBOCYTE LYSATE TEST
INTERNATIONAL CONFERENCE WOODS HOLE MASSACHUSETTS USA SEPTEMBER 8-11 1985.
AU WATSON S W [Reprint author]; LEVIN J; NOVITSKY T J
CS WOODS HOLE OCEANOGRAPHIC INST, WOODS HOLE, MASSACHUSETTS, USA
SO Prog. Clin. Biol. Res., (1987) pp. XIX+528P. WATSON, S. W., J. LEVIN AND T. J. NOVITSKY (ED.). PROGRESS IN CLINICAL AND BIOLOGICAL RESEARCH, VOL. 231. DETECTION OF BACTERIAL ENDOTOXINS WITH LIMULUS AMEBOCYTE LYSATE TEST; INTERNATIONAL CONFERENCE, WOODS HOLE, MASSACHUSETTS, USA, SEPTEMBER 8-11, 1985. XIX+528P. ALAN R. LISS, INC.: NEW YORK, NEW YORK, USA. ILLUS.
Publisher: Series: Progress in Clinical and Biological Research.
CODEN: PCBRD2. ISSN: 0361-7742. ISBN: 0-8451-5081-2.
DT Book
Conference; (Meeting)
FS BR
LA ENGLISH
ED Entered STN: 27 Sep 1987
Last Updated on STN: 27 Sep 1987
CC General biology - Symposia, transactions and proceedings 00520
Biochemistry studies - Lipids 10066
Biochemistry studies - Carbohydrates 10068
Toxicology - General and methods 22501
Physiology and biochemistry of bacteria 31000
Microbiological apparatus, methods and media 32000
Medical and clinical microbiology - General and methods 36001
Medical and clinical microbiology - Bacteriology 36002
IT Major Concepts
Infection; Toxicology
IT Miscellaneous Descriptors
BOOK MEETING
ORGN Classifier
Bacteria 05000
Super Taxa
Microorganisms
Taxa Notes
Bacteria, Eubacteria, Microorganisms

L28 ANSWER 12 OF 14 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN 1987:119991 BIOSIS
DN PREV198732059108; BR32:59108
TI DEVELOPMENT AND APPLICATION OF THE LIMULUS AMEBOCYTE LYSATE TEST FOR BACTERIAL ENDOTOXINS PYROGENS.
AU NOVITSKY T J [Reprint author]
CS ASSOCIATES OF CAPE COD, INC, WOODS HOLE, MASSACHUSETTS 02543, USA
SO Medical Laboratory Sciences, (1986) Vol. 43, No. SUPPL. 1, pp. S51.
Meeting Info.: EIGHTEENTH TRIENNIAL CONFERENCE OF THE INSTITUTE OF MEDICAL LABORATORY SCIENCES, SOUTHAMPTON, ENGLAND, AUG. 18-22, 1986. MED LAB SCI.
CODEN: MLASDU. ISSN: 0308-3616.
DT Conference; (Meeting)
FS BR
LA ENGLISH
ED Entered STN: 28 Feb 1987
Last Updated on STN: 28 Feb 1987
CC General biology - Symposia, transactions and proceedings 00520
Biochemistry methods - General 10050
Biochemistry studies - General 10060
Biochemistry studies - Lipids 10066
Biochemistry studies - Carbohydrates 10068
Pathology - Diagnostic 12504
Toxicology - General and methods 22501
Physiology and biochemistry of bacteria 31000
Microbiological apparatus, methods and media 32000
Medical and clinical microbiology - General and methods 36001
Medical and clinical microbiology - Bacteriology 36002

IT Major Concepts
Infection; Pathology; Toxicology
IT Miscellaneous Descriptors
ABSTRACT CLINICAL APPLICATIONS
ORGN Classifier
Bacteria 05000
Super Taxa
Microorganisms
Taxa Notes
Bacteria, Eubacteria, Microorganisms

L28 ANSWER 13 OF 14 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN **1986:5504** BIOSIS
DN PREV198630005504; BR30:5504
TI QUANTIFICATION OF **ENDOTOXIN** INHIBITION IN SERUM AND PLASMA USING A TURBIDIMETRIC **LIMULUS AMEBOCYTE** LYSATE ASSAY.
AU **NOVITSKY T J** [Reprint author]; ROSLANSKY P F
CS ASSOCIATES OF CAPE COD, INC, WOODS HOLE, MASSACHUSETTS 02543, USA
SO Prog. Clin. Biol. Res., (**1985**) pp. 181-194. TEN CATE, J. W. ET AL. (ED.). PROGRESS IN CLINICAL AND BIOLOGICAL RESEARCH, VOL. 189. BACTERIAL ENDOTOXINS: STRUCTURE, BIOMEDICAL SIGNIFICANCE, AND DETECTION WITH THE LIMULUS AMEBOCYTE LYSATE TEST; INTERNATIONAL CONFERENCE ON ENDOTOXIN ASSAYS, AMSTERDAM, NETHERLANDS, MAY 25-26, 1984. XIX+466P. ALAN R. LISS, INC.: NEW YORK, N.Y., USA. ILLUS.
Publisher: Series: Progress in Clinical and Biological Research.
CODEN: PCBRD2. ISSN: 0361-7742. ISBN: 0-8451-5039-1.
DT Book
Conference; (Meeting)
FS BR
LA ENGLISH
ED Entered STN: 25 Apr 1986
Last Updated on STN: 25 Apr 1986
CC General biology - Symposia, transactions and proceedings 00520
Methods - Laboratory methods 01004
Biochemistry methods - General 10050
Biochemistry studies - Lipids 10066
Biochemistry studies - Carbohydrates 10068
Biophysics - Molecular properties and macromolecules 10506
External effects - Temperature as a primary variable - hot 10618
Pathology - Diagnostic 12504
Blood - Blood and lymph studies 15002
Toxicology - General and methods 22501
Temperature - General measurement and methods 23001
Morphology and cytology of bacteria 30500
Physiology and biochemistry of bacteria 31000
Microbiological apparatus, methods and media 32000
Medical and clinical microbiology - General and methods 36001
Medical and clinical microbiology - Bacteriology 36002
IT Major Concepts
Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Infection; Pathology; Toxicology
IT Miscellaneous Descriptors
HUMAN HEAT DILUTION NEUTRALIZATION
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

L28 ANSWER 14 OF 14 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN **1983:315739** BIOSIS
DN PREV198376073231; BA76:73231
TI DETECTION OF ENDO TOXIN IN ANTIBIOTIC SOLUTIONS WITH **LIMULUS**

AMOEBOCYTE LYSATE.
AU CASE M J [Reprint author]; RHYTHER S S; NOVITSKY T J
CS ASSOCIATES CAPE COD, INC, WOODS HOLE, MASS 02543, USA
SO Antimicrobial Agents and Chemotherapy, (1983) Vol. 23, No. 5, pp. 649-652.
CODEN: AMACCQ. ISSN: 0066-4804.
DT Article
FS BA
LA ENGLISH
AB Twenty-eight antibiotics were tested with the **Limulus amoebocyte** lysate assay to determine their non-inhibitory concentrations (NIC). The **Limulus amoebocyte** lysate assay was a valid test for most of the antibiotics tested; the NIC were greater than the minimum valid test concentrations. Borderline results were obtained with cefamandole nafate and neomycin sulfate. Polymyxin B and colistimethate contained too much **endotoxin** to permit determination of NIC. The NIC of tetracycline hydrochloride was dependent on the initial concentration of antibiotic. This dependence was most likely caused by the amount of base required to adjust the pH before testing.
CC Biochemistry methods - Lipids 10056
Biochemistry methods - Carbohydrates 10058
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Lipids 10066
Biochemistry studies - Carbohydrates 10068
Pharmacology - General 22002
Toxicology - General and methods 22501
Toxicology - Pharmacology 22504
Physiology and biochemistry of bacteria 31000
Microbiological apparatus, methods and media 32000
Medical and clinical microbiology - Bacteriology 36002
Public health - Public health laboratory methods 37006
Public health: disease vectors - Inanimate 37060
Public health: microbiology - Public health microbiology 37400
Chemotherapy - General, methods and metabolism 38502
IT Major Concepts
Infection; Methods and Techniques; Pharmacology; Toxicology
IT Miscellaneous Descriptors
CEFAMANDOLE NAFATE NEOMYCIN SULFATE POLYMYXIN B COLISTIMETHATE TETRACYCLINE HYDRO CHLORIDE
ORGN Classifier
Bacteria 05000
Super Taxa
Microorganisms
Taxa Notes
Bacteria, Eubacteria, Microorganisms
ORGN Classifier
Merostomata 75404
Super Taxa
Chelicerata; Arthropoda; Invertebrata; Animalia
Taxa Notes
Animals, Arthropods, Chelicerates, Invertebrates
RN 42540-40-9 (CEFAMANDOLE NAFATE)
1405-10-3 (NEOMYCIN SULFATE)
1404-26-8 (POLYMYXIN B)
8068-28-8 (COLISTIMETHATE)
64-75-5 (TETRACYCLINE HYDROCHLORIDE)
34444-01-4 (CEFAMANDOLE)

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(FILE 'HOME' ENTERED AT 10:45:39 ON 25 SEP 2006)

FILE 'HCAPLUS' ENTERED AT 10:46:13 ON 25 SEP 2006
L1 4 US2005026239/PN OR (US2004-826922 OR US2003-463737#)/AP,PRN

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L2            83 E3-8
                E CASTRO CARLOS/AU
L3            42 E3-5
                E RIDGE R/AU
L4            44 E3-4,E8-9
                E NOVITSKY T/AU
L5            47 E4,E6-7
L6           156 (CAPE COD)/CS,PA
                E TOXINS/CT
                E E3+ALL
L7          8911 E2+OLD,NT (L)?ENDOTOXIN?
L8           482 L7 (L) ANT/RL
                E LIMULUS POLYPHEMUS/CT
                E E3+ALL
L9           852 E7
L10           20 L8 AND L9
L11            4 L10 AND L1-6
L12           16 L10 NOT L11
L13           13 L12 AND (PY<=2003 OR PRY<2003 OR AY<=2003)
L14            3 L13 AND (GELCLOT? OR GEL CLOT?)
                SEL AN 1-2 L12
L15            2 E1-4 AND L12
L16           19 L11,L13-15

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                E CASTRO C/AU
L17          345 E3-34
                E CASTRO CARLOS/AU
L18            2 E3-4
                E RIDGE R/AU
L19           23 E3-4
L20            6 E8-9
                E NOVITSKY T/AU
L21           75 E3-8
L22            1 L17-21 AND 75000/BC
L23           51 L17-21 AND (LAL OR AMOEBOCYTE? OR AMEBOCYTE? OR LIMULUS)
L24           50 L23 AND PY<=2003
L25           40 L24 AND ?ENDOTOXIN?
                SEL AN L25 6 7 10 13 23-25 29-30 31 34 36 39
L26           13 E1-13 AND L25
L27            2 L25 AND (GELCLOT? OR GEL CLOT?)
L28           14 L26-27

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FILE LAST UPDATED:          22 SEP 2006      <20060922/UP>
MOST RECENT DERWENT UPDATE:     200661        <200661/DW>
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http://www.stn-international.de/stndatabases/details/ipc_reform.html and
http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf <<<

>>> FOR FURTHER DETAILS ON THE FORTHCOMING DERWENT WORLD PATENTS
    INDEX ENHANCEMENTS PLEASE VISIT:
http://www.stn-international.de/stndatabases/details/dwpi_r.html <<<
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L16 ANSWER 1 OF 7 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
AN 2004-795646 [78] WPIX
DNN N2004-627055 DNC C2004-277789
TI Test kit for detecting bacterial **endotoxin** in aqueous solution, comprises first containers containing horseshoe crab amebocyte lysate, second containers containing **endotoxin**, and disposable **endotoxin**-free transfer instruments.
DC B04 D16 S03
IN **CASTRO, C A; NOVITSKY, T J; RIDGE, R J**
PA **(ASCA-N) ASSOC CAPE COD INC**; (CAST-I) CASTRO C A; (NOVI-I) NOVITSKY T J; (RIDG-I) RIDGE R J
CYC 108
PI WO--2004094987 A2 20041104 (200478)* EN 18 G01N-000-00
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
US--2005026239 A1 20050203 (200511) C12Q-001-04
US--2005048655 A1 20050303 (200517) G01N-033-554
US--2005069972 A1 20050331 (200524) C12Q-001-04
EP-----1627040 A2 20060222 (200615) EN C12M-001-34
R: DE FR GB IT NL
ADT WO--2004094987 A2 2004WO-US011917 20040413; US--2005026239 A1 Provisional 2003US-463737P 20030418, 2004US-0826922 20040419; US--2005048655 A1 Provisional 2003US-463737P 20030418, CIP of 2004US-0826922 20040419, 2004US-0867162 20040614; US--2005069972 A1 Provisional 2003US-463737P 20030418, CIP of 2004US-0826922 20040419, CIP of 2004US-0867162 20040614, 2004US-0897979 20040723; EP-----1627040 A2 2004EP-0750270 20040419, 2004WO-US11917 20040419
FDT EP-----1627040 A2 Based on WO--2004094987
PRAI 2003US-463737P 20030418; 2004US-0826922 20040419; 2004US-0867162 20040614; 2004US-0897979 20040723
IC ICM C12M-001-34; C12Q-001-04; G01N-000-00; G01N-033-554
ICS C12Q-001-22; C12Q-001-34; G01N-031-00; **G01N-033-53**; G01N-033-569
AB WO2004094987 A UPAB: 20041206
NOVELTY - A test kit comprises first container(s) containing freeze dried, **endotoxin**-specific, horseshoe crab amebocyte lysate such that the sensitivity of the lysate is pre-certified, second container(s) containing **endotoxin** to serve as a positive control, where the defined quantity of **endotoxin** is pre-certified to positively react with the amebocyte lysate present in the first container, and disposable **endotoxin**-free transfer instrument(s).

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method for specifically detecting bacterial **endotoxin** in an aqueous solution, comprising using a defined quantity of **endotoxin** to serve as a positive control, where the defined quantity of **endotoxin** is pre-certified to positively react with the horseshoe crab amebocyte lysate, and the sensitivity of the gel clot method can vary based on the time of incubation of the test.

USE - The test kit is for detecting bacterial **endotoxin** in an aqueous solution using a gel-clot method. It is used in renal dialysis clinic.

ADVANTAGE - The inventive test kit is simple, rapid, and cost-effective. It combines the ease of using gel-clot assay with the speed and multi-sensitivity of the photometric methods, but without requiring specialized equipment or expertise.

Dwg.0/0
FS CPI EPI

FA AB
MC CPI: B04-B04D; B04-C02V; B04-F04; B11-C03; B11-C06; B11-C09; D05-H04; D05-H09
EPI: S03-E09E; S03-E14H
TECH UPTX: 20041206
TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Method: The aqueous solution is purified, distilled, sterile, non-sterile, or filtered water, water for injection, water for irrigation, or reverse osmosis water. The aqueous solution is dialysate. The sensitivity of the gel clot method can vary based on the formulation of the amebocyte lysate. Preferred Components: The first and second containers are test tubes having 12 by 75 mm and round-bottomed. The disposable **endotoxin** -free transfer instrument is a pipette. The test kit further comprises written instructions for carrying out the test, and written certificate of analysis of the amebocyte lysate sensitivity, the quantity of **endotoxin** in the positive control, and/or the **endotoxin** -free nature of the transfer instrument.
TECHNOLOGY FOCUS - BIOLOGY - Preferred Components: The horseshoe crab amebocyte lysate is from **Limulus** polyphemus. Preferred Parameters: The quantity of **endotoxin** is two times the sensitivity of the amebocyte lysate. The level of sensitivity of the test kit for detecting **endotoxin** can vary based on the formulation of the amebocyte lysate in container one and the incubation time of containers one and two. The amebocyte lysate is 0.4, or 0.6, preferably 0.5 ml.

L16 ANSWER 2 OF 7 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
AN 2004-167218 [16] WPIX
CR 1992-415712 [50]; 1997-107149 [10]; 1997-201472 [18]; 1997-271365 [24]; 1998-285799 [25]; 2002-265890 [31]; 2002-555994 [59]
DNN N2004-133276 DNC C2004-066343
TI Isolating **endotoxin** binding protein from horseshoe crab by obtaining cell debris from amebocytes, extracting cell debris with denaturant to produce extract, obtaining solution having **endotoxin** binding protein.
DC A89 B04 D16 S03
IN **NOVITSKY, T J**; WAINWRIGHT, N R
PA (NOVI-I) NOVITSKY T J; (WAIN-I) WAINWRIGHT N R
CYC 1
PI US--2003229211 A1 20031211 (200416)* 29 C07K-001-16
ADT US--2003229211 A1 Div ex 1988US-0210575 19880623, CIP of 1990US-0480957 19900216, CIP of 1991US-0701501 19910516, Cont of 1992US-0883457 19920515, Div ex 1994US-0264244 19940622, Div ex 1995US-0476940 19950607, Div ex 1997US-0850011 19970501, 2001US-0998780 20011203
FDT US--2003229211 A1 Div ex US-----5594113, Div ex US-----5627266, Div ex US-----6384200
PRAI 1992US-0883457 19920515; 1988US-0210575 19880623;
1990US-0480957 19900216; 1991US-0701501 19910516;
1994US-0264244 19940622; 1995US-0476940 19950607;
1997US-0850011 19970501; 2001US-0998780 20011203
IC ICM C07K-001-16
AB US2003229211 A UPAB: 20040305
NOVELTY - Isolating (M1) **endotoxin** binding protein (I) from horseshoe crab by subjecting amebocytes from horseshoe crab to hypotonic shock and obtain cell debris, extracting cell debris with denaturant to produce extract, passing it through filtration membrane to obtain filtrate, concentrating filtrate, subjecting retentate to chromatography, eluting solution having **endotoxin** binding activity.
DETAILED DESCRIPTION - Isolating (M1) **endotoxin** binding protein (I) from a horseshoe crab involves subjecting amebocytes obtained from horseshoe crab to hypotonic shock to lyse the amebocytes and obtain cell debris from the lysed amebocytes, extracting the cell debris with a solution containing a denaturant such as urea or guanidine hydrochloride to produce an extract, passing the extract through a first ultrafiltration membrane having a molecular cutoff of from 20000 to 50000 Da to obtain a filtrate, concentrating the filtrate by passing it through a second

ultrafiltration membrane having a molecular cutoff of from 5000-10000 to produce a retentate, subjecting the retentate to cation exchange chromatography at a pH of 5-6 using an elution buffer which comprises urea, eluting a solution containing a peak of **endotoxin** binding activity and applying the solution to a reverse phase column, and adding a buffer to the column, to obtain a solution containing purified (I).

INDEPENDENT CLAIMS are also included for the following:

(1) a product produced by (M1) having **endotoxin** binding capability and being a protein having an initial amino acid sequence chosen from Ser-Asn-Ile-Trp-Thr-, Asp-Asn-, Ser-Gly-, and Ser-Asn-;

(2) a pharmaceutical composition for ameliorating the biological effects of **endotoxin** in vivo when administered to a mammal, comprising purified (I) and a carrier, where (I) has a fully defined sequence of 101 amino acids (S1) as given in the specification or an amino acid sequence corresponding to amino acid position 30-55 of a fully defined sequence of 105 amino acids (S2) as given in the specification and up to complete (S2);

(3) (I) having (S1) free of the contaminating components naturally associated with the horseshoe crab, or (S2); and

(4) a DNA molecule encoding (I) and free of the contaminating components naturally associated with the horseshoe crab.

ACTIVITY - Vasotropic; Antibacterial; Immunosuppressive; Antiarthritic; Antiinflammatory.

MECHANISM OF ACTION - Inactivator of **endotoxin**. In vivo therapeutic efficacy of **Limulus endotoxin** binding protein was assayed as follows. Escherichia coli **endotoxin** was injected intravenously into 9 rabbits at a dose of 50 ng/kg. After 15 minutes, three were injected intravenously with 5 micro g **Limulus endotoxin** binding protein and three received phosphate buffered saline (PBS). Volumes of all injections were 0.5 ml/kg. Body temperatures were monitored for 6 hours and data collected every 10 minutes. Animals received **endotoxin** and the PBS only, manifested the normal peak fever response one hour after toxin administration. Those animals received therapeutic injections of the **Limulus** protein exhibited a much reduced fever response proportional to the amount of protein which was administered.

USE - (M1) is useful for isolating **endotoxin** binding protein from a horseshoe crab **Limulus** polyphemus. (I) is useful for ameliorating the biological effects of **endotoxin** in vivo which involves administering (I) to a mammal such as human in need of such treatment. (I) is useful for assaying **endotoxin** concentration which involves contacting serial aqueous dilutions of a material such as biological fluid suspected of containing **endotoxin** with a known quantity of (I), observing the fluorescence emission of a wavelength of (I) before and after contact with the aqueous dilutions of the material suspected of containing **endotoxin** and correlating the level of fluorescence emission with a known emission level to determine the quantity of **endotoxin** present in the material suspected of containing **endotoxin**, where the fluorescence emission produced by excitation from 275-295 nm, is measured at 340-360 nm. (I) is useful for reducing **endotoxin** contamination of a material suspected of containing **endotoxin**, which involves contacting the material with the **endotoxin** binding molecule of (I) to form a complex between **endotoxin** and the **endotoxin** binding molecule, and separating the complex from the sample. (I) is also useful for extracorporeally removing **endotoxin** from blood which involves contacting blood with immobilized (I), and for assaying **endotoxin** concentration in a material suspected of containing **endotoxin** which involves contacting the material with a biosensor device comprising (I) immobilized on a solid phase support, detecting a change in capacitance, resistance, or acoustic wave of the solid phase support, and correlating the change with the changes observed with standard solutions of (I) (claimed). (I) is useful for treating diseases such as septicemia, toxic shock, gram-negative bacterial infections, **endotoxin** -related arthritis, gonorrhea, periodontal disease, spinal meningitis, infections of amniotic fluid and for treatment of septic shock.

DESCRIPTION OF DRAWING(S) - The figure shows a plot of apparent **endotoxin** concentration versus protein concentration.
Dwg.3/16
FS CPI EPI
FA AB; GI
MC CPI: A12-L04A; B04-C01G; B04-F01; B04-N02A; B04-N02A0E; B11-C08D2; B11-C08D3; **B12-K04**; **B12-K04E**; B14-A01; B14-A01A; B14-C03; B14-C09; B14-F02; B14-J01; B14-L06; B14-S06; D05-H08; **D05-H09**; D05-H13
EPI: S03-E14H5
ABEX UPTX: 20040305
ADMINISTRATION - (I) is administered orally, parenterally, or intravenously. Dosage ranges from 1000-5000 units/ng, preferably 0.1-100 mg/kg of body weight per day per patient of measured **endotoxin**.

EXAMPLE - No relevant example is given.
TECH UPTX: 20040305
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: In (M1), the hypotonic shock is accomplished by treating the amebocytes with **endotoxin**-free distilled water at 0-10 degreesC. The extraction of cell debris is accomplished with 6 molar urea or guanidine hydrochloride. The ultrafiltration membranes are each composed of polysulfone. The extract is crudely filtered with filter aid chosen from diatomaceous earth, cationic and anionic colloidal particle suspensions, before passing the extract through the ultrafiltration membrane. The first and second polysulfone membranes have a molecular cutoff of 30000 and 8000 Da, respectively. The cation exchange chromatography is accomplished with sepharose. The cation exchange step involves elution from the cation exchange column with a step gradient of salt chosen from ammonium chloride, potassium chloride and sodium chloride. The above mentioned step also involves elution with a buffer containing 1-6 molar urea. The reversed phase column is a resin having 4,8, or 18 C chains and is eluted with a step gradient of isopropanol and trifluoroacetic acid which has a concentration ranging from 0.15-0.25%.
Preferred Protein: (I) is immobilized on a solid phase support such as chromatographic resin or a membrane. The immobilized (I) is a biosensor device, where the solid phase support is quartz or silicon.

L16 ANSWER 3 OF 7 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
AN 2002-555994 [59] WPIX
CR 1990-022516 [03]; 1992-415712 [50]; 1997-107149 [10]; 1997-201472 [18]; 1997-271365 [24]; 1998-285799 [25]; 2002-265890 [31]; 2004-167218 [16]
DNC C2002-157595
TI Isolation of **endotoxin**-binding protein, useful e.g. for treating sepsis and detecting **endotoxin**, from cellular debris of lysed horseshoe crab amebocytes.
DC A96 B04
IN **NOVITSKY, T J**; WAINWRIGHT, N R
PA **(ASCA-N) ASSOC CAPE COD INC**
CYC 1
PI US-----6384200 B1 20020507 (200259)* 29 C07K-001-14
ADT US-----6384200 B1 Div ex 1988US-0210575 19880623, CIP of 1990US-0480957 19900216, CIP of 1991US-0701501 19910516, Cont of 1992US-0883457 19920515, Div ex 1994US-0264244 19940622, Div ex 1995US-0476940 19950607, 1997US-0850011 19970501
FDT US-----6384200 B1 Div ex US-----5594113, Div ex US-----5627266
PRAI 1992US-0883457 19920515; 1988US-0210575 19880623; 1990US-0480957 19900216; 1991US-0701501 19910516; 1994US-0264244 19940622; 1995US-0476940 19950607; 1997US-0850011 19970501
IC ICM C07K-001-14
ICS C07K-001-34
AB US 6384200 B UPAB: 20040305
NOVELTY - Isolating **endotoxin**-binding protein (I) from a horseshoe crab comprises lysing amebocytes by hypotonic shock. The cell debris is recovered and extracted with a solution containing denaturant

(urea or guanidine hydrochloride). The extract is passed through an ultrafiltration (UF) membrane and the filtrate concentration by passing through a second UF membrane.

DETAILED DESCRIPTION - Isolating **endotoxin**-binding protein (I) from a horseshoe crab comprises lysing amebocytes by hypotonic shock. Then the cell debris is recovered and extracted with a solution containing denaturant (urea or guanidine hydrochloride). The extract is passed through an ultrafiltration (UF) membrane of molecular weight cut-off 20-50 kD and the filtrate concentration by passing through a second UF membrane of molecular weight cut-off 5-10 kD. The retentate is subjected to cation-exchange chromatography (CEC) at pH 5-6, eluting with a urea-containing buffer and the (I)-containing peak applied to a reverse-phase column. This is eluted with buffer to recover a solution containing purified (I).

ACTIVITY - Antibacterial; Immunosuppressive; Antiinflammatory; Antiarthritic.

When male rats were injected intravenously with 15 mg/kg of lipopolysaccharide (LPS) from Escherichia coli 0111:B4, 14 of 20 were dead within 24 hours. When animals were injected with a mixture of 15 mg/kg each of LPS and (I), incubated together for 1 hour before administration, all 20 survived.

MECHANISM OF ACTION - None given in the source material.

USE - (I) is used to treat or prevent the effects of **endotoxin** in vivo, e.g. for treating or preventing sepsis caused by Gram-negative bacteria, **endotoxin**-related arthritis, gonorrhea, periodontal disease, spinal meningitis and infections of amniotic fluid, in human or veterinary medicine. (I) can also be used in vitro to remove **endotoxin**, e.g. from pharmaceuticals or in extracorporeal treatment of sepsis and in an assay for **endotoxin** e.g. checking water purity or for contamination in pharmaceutical preparations.

ADVANTAGE - (I) can be administered before or after exposure to **endotoxin**; has very high binding affinity, and, since it is relatively small, is unlikely to be antigenic. When used for detection of **endotoxin**, (I) eliminates the need for dilution (as required in the conventional **Limulus** amebocyte lysate test) and makes possible the development of a portable biosensor for use in the field.

Dwg.0/16

FS CPI

FA AB; DCN

MC CPI: A05-J06; A12-W11A; B04-N04; **B12-K04**; B14-S06

ABEX UPTX: 20020916

ADMINISTRATION - The dosage is 0.1-100 mg/kg/day intravenously.

EXAMPLE - No relevant examples are given.

TECH UPTX: 20020916

TECHNOLOGY FOCUS - BIOLOGY - Preferred process: Amebocytes are lysed in **endotoxin**-free distilled water at 0-10degreesC, and extraction of cellular debris is with a 6M denaturant solution. The extract is coarsely filtered through a filter aid (diatomaceous earth or suspensions of cationic or anionic particles) before UF, which is especially with 30 and 8 kD cut-off membranes. CEC is on crosslinked agarose, eluting with either a step gradient of ammonium, potassium of sodium chlorides or with a buffer containing 1-6 M urea. The reverse-phase step is on a C4, 8 or 18 column, eluting with a step gradient of isopropanol and trifluoroacetic acid (at 0.15-0.25%).

Preferred materials: The amebocytes are from **Limulus** polyphemus. (I) is a 101 amino acid amphipathic protein (reproduced) that has high affinity for the lipid A component of **endotoxin**.

L16 ANSWER 4 OF 7 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN

AN 2002-265890 [31] WPIX

CR 1990-022516 [03]; 1992-415712 [50]; 1997-107149 [10]; 1997-201472 [18]; 1997-271365 [24]; 1998-285799 [25]; 2002-555994 [59]; 2004-167218 [16]

DNN N2002-206464 DNC C2002-079191

TI Novel **endotoxin** binding protein fragment free of contaminating

components naturally associated with horseshoe crab, for e.g. treating septicemia, toxic shock, gram-negative bacterial infections, gonorrhea and arthritis.

DC B04 S03

IN **NOVITSKY, T J**; WAINWRIGHT, N R

PA **(ASCA-N) ASSOC CAPE COD INC**

CYC 1

PI US-----6222021 B1 20010424 (200231)* 28 G01N-033-48 <--

ADT US-----6222021 B1 Div ex 1988US-0210575 19880623, CIP of 1990US-0480957 19900216, CIP of 1991US-0701501 19910516, Cont of 1992US-0883457 19920515, Div ex 1994US-0264244 19940622, Cont of 1996US-0704872 19960830, 1997US-0871600 19970609

FDT US-----6222021 B1 Div ex US-----5594113, Cont of US-----5747455

PRAI 1992US-0883457 19920515; 1988US-0210575 19880623;
1990US-0480957 19900216; 1991US-0701501 19910516;
1994US-0264244 19940622; 1996US-0704872 19960830;
1997US-0871600 19970609

IC ICM **G01N-033-48**
ICS C07K-001-00

AB US 6222021 B UPAB: 20040305

NOVELTY - A fragment (I) of an **endotoxin** binding protein having a sequence (S) of 105 amino acids fully defined in the specification consisting of at least amino acids 34-59 of (S), where (I) is free of the contaminating components naturally associated with the horseshoe crab, is new.

ACTIVITY - Immunosuppressive; antibacterial; antiarthritic; antiinflammatory.

Escherichia coli **endotoxin** was injected intravenously into 9 rabbits at a dose of 50 ng/kg. After 15 minutes, 3 each were injected intravenously with 5, and 50 micro g **Limulus Endotoxin** Binding Protein, and 3 received phosphate buffered saline (PBS). Volumes of all injections were 0.5 ml/kg. Body temperatures were monitored for 6 hours and data was collected every 10 minutes. Animals which received **endotoxin** and the PBS only, manifested the normal peak fever response one hour after toxin administration. The animals which received therapeutic injections of the **Limulus** protein exhibited a much reduced fever response proportional to the amount of protein administered.

MECHANISM OF ACTION - None given.

USE - (I) is useful in an assay for **endotoxin**, for exerting a protective effect against the effects of **endotoxin**, for treating an animal in vivo, so as to exert a therapeutic effect if **endotoxin** is present in the animal, or to exert a protective or preventive effect, if the animal should come to contact with **endotoxin** later. (I) is useful for treating septicemia, toxic shock, gram-negative bacterial infections accompanied by an increase in in vivo **endotoxin** content, **endotoxin**-related arthritis, gonorrhea, periodontal diseases, spinal meningitis, and infections of amniotic fluid. (I) is useful for veterinary purposes to reduce or prevent the pyrogenic or other ill effects of **endotoxin** in vivo in, for e.g., dogs, cats, horses, cattle, sheep, and rabbits, and to prevent or reduce effects of **endotoxin** in laboratory animals such as mice and rats.

Dwg.0/16

FS CPI EPI

FA AB; DCN

MC CPI: B04-N04; B05-B02C; B14-A01A; B14-A01A5; B14-C03; B14-N06B; B14-N14; B14-N16; B14-S06
EPI: S03-E14H

ABEX UPTX: 20020516

ADMINISTRATION - (I) is administered by oral, parenteral, intravenous, intradermal, subcutaneous, or topical route at a dose of 0.1-100 mg/kg.

TECH UPTX: 20020516

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Fragment: (I) consists of a sequence corresponding to amino acid positions 34-59 of (S). (I) is immobilized on a solid phase support such as a chromatographic resin or a membrane, quartz or silicon. The immobilized **endotoxin** binding

protein fragment is a biosensor device.

L16 ANSWER 5 OF 7 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
AN 2000-180947 [16] WPIX
DNC C2000-056417
TI Measuring **endotoxin** level in a test sample comprises contacting an amebocyte lysate with beta-1,4-glucan to inhibit the glucan-sensitive enzymatic pathway in the lysate and reduce the number of false positives.
DC A96 B04 D16
IN LOVEROCK, B
PA (BIOW-N) BIOWHITTAKER TECHNOLOGIES INC; (BIOW-N) BIOWHITAKER TECHNOLOGIES
CYC 2
PI US-----5998389 A 19991207 (200016)* 10 A61K-031-715
JP--2000002708 A 20000107 (200016) 8 G01N-033-579
ADT US-----5998389 A 1998US-0081659 19980520; JP--2000002708 A 1999JP-0139410 19990520
PRAI 1998US-0081659 19980520
IC ICM A61K-031-715; G01N-033-579
ICS C12Q-001-00; C12Q-001-04
AB US 5998389 A UPAB: 20000330
NOVELTY - Measuring **endotoxin** in a test sample comprises contacting an amebocyte lysate with beta -1,4-glucan with beta -1,4-glycoside linkages (I), to inhibit the glucan-sensitive enzymatic pathway in the lysate.
DETAILED DESCRIPTION - A method for measuring **endotoxin** in a test sample using an amebocyte lysate comprises contacting the lysate with beta -1,4-glucan with beta -1,4-glycoside linkages (I), to inhibit the glucan-sensitive enzymatic pathway in the lysate and detecting the **endotoxin** by a kinetic chromogenic method, an end point chromogenic method, a **gel-clot** method, a turbidimetric method or enzyme linked immunosorbent assay.
INDEPENDENT CLAIMS are also included for the following:
(1) reagent for specifically detecting presence of **endotoxin** in test sample comprising (I) and amebocyte lysate; and
(2) a kit for detecting the presence of **endotoxin** in test sample comprising (I), amebocyte lysate and instruction for using the kit.
USE - Using (I) in the **endotoxin** assay reduces the number of false positives caused by the glucan-sensitive enzymatic pathway in amebocyte lysate (claimed). The method can be used to detect **endotoxin** contamination of water, medial devices, pharmaceuticals and biological test samples such as blood, tissue culture medium and serum.
ADVANTAGE - The false positive results due to (I) contamination is effectively removed and the **endotoxin** level in the sample is measured accurately.
Dwg.0/3
FS CPI
FA AB; DCN
MC CPI: A03-A00A; A12-V03C2; B04-B04M; B04-C02V; B04-D01; B04-F07; B11-C07A4; B11-C08D; **B12-K04A**; D05-A01A4; D05-A01B; **D05-H09**
ABEX UPTX: 20000330
EXAMPLE - The response of **endotoxin** assay to **Limulus** amebocyte lysate (LAL) raw water, purified EC-6 **endotoxin** native Escherichia coli **endotoxin**, LAL-reactive material (LAL-RM) and Zymosan A was measured in **gel clot** assay in the presence and absence of 35 mg/ml cellobiose. Positive results were obtained to both purified EC-6 **endotoxin** and E. coli **endotoxin**. In the absence of cellobiose **gel clots** were formed in response to both LAL-RM and Zymosan A. The presence of cellobiose in the assay inhibited **gel clot** formation in response to LAL-RM and Zymosan A. These results indicated that the glucan responsive pathway in an LAL was inhibited by the presence of cellobiose in a **gel clot** assay.
TECH UPTX: 20000330
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: (I) is a polymer comprising two or more glucose monomers and is preferably cellobiose used

in an amount of 100 mg/ml-100 mg/ml and more preferably 15 mg/ml-25 mg/ml. At last one of the hydroxyl groups of (I) is modified by an alkyl, carboxy methyl, methyl or hydroxyl propyl group. (I) is premixed with the test sample before or after contacting with the amebocyte lysate. The lysate can be lyophilized and reconstituted either before or after the step of contacting the lysate.
Preferred Sample: The amebocyte lysate is prepared from amebocyte of horse shoe crabs **Limulus** polyphemus; Tachypleus tridentatus; T. gigas or Carcinoscorpius rotundicauda.

L16 ANSWER 6 OF 7 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
AN 1997-201472 [18] WPIX
CR 1990-022516 [03]; 1992-415712 [50]; 1997-107149 [10]; 1997-271365 [24]; 1998-285799 [25]; 2002-265890 [31]; 2002-555994 [59]; 2004-167218 [16]
DNC C1997-064379
TI Assaying **endotoxin** using binding protein from horseshoe crab - and measuring quenching of tryptophan fluorescence caused by **endotoxin** binding.
DC B04 D16
IN **NOVITSKY, T J**; WAINWRIGHT, N R
PA **(ASCA-N) ASSOC CAPE COD INC**
CYC 1
PI US-----5614369 A 19970325 (199718)* 29 C12Q-001-00
ADT US-----5614369 A Div ex 1988US-0210575 19880623, CIP of 1990US-0480957 19900216, CIP of 1991US-0701501 19910516, Cont of 1992US-0883457 19920515, Div ex 1994US-0264244 19940622, 1995US-0478689 19950607
PRAI 1992US-0883457 19920515; 1988US-0210575 19880623;
1990US-0480957 19900216; 1991US-0701501 19910516;
1994US-0264244 19940622; 1995US-0478689 19950607
IC ICM C12Q-001-00
ICS C07K-014-00
AB US 5614369 A UPAB: 20040305
Assaying **endotoxin** concentration, comprises: (a) contacting serial aqueous dilutions of test sample with a known amount of a **endotoxin** binding protein having the 105 residue amino acid sequence given in the specification; (b) measuring the fluorescence emission, at least 1 wavelength, from the protein before and after contact; and (c) correlating the levels of emission with known emission levels, to determine the quantity of **endotoxin** present.
USE - The method can be used to determine water purity and process cleanliness during pharmaceutical manufacture, to check kidney dialysis units and generally wherever the **Limulus** amoebocyte lysate (LAL) assay is currently used. Also the protein, or a truncated version lacking the 1st 4 amino acids, can be used therapeutically to bind/neutralise **endotoxin** in vivo (e.g. in cases of septicaemia, toxic shock, **endotoxin** related arthritis, gonorrhoea, periodontal disease, spinal meningitis and amniotic fluid infection), and to remove **endotoxin** from solutions (e.g. extracorporeal treatment of septic shock).
ADVANTAGE - The protein has a very high binding constant for a wide range of bacterial **endotoxins**, and being of low molecular weight is likely to be less immunogenic than anti-**endotoxin** antibodies. The protein also avoids the multiple interferences associated with the conventional LAL assay.
Dwg.6/16
FS CPI
FA AB; GI
MC CPI: B04-N02; B04-N03; B11-C07B3; **B12-K04**; B14-A01A5; B14-C09; B14-N03; B14-N06B; B14-N16; B14-S06; **D05-H09**; D05-H12A; D05-H17A6

L16 ANSWER 7 OF 7 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
AN 1990-022516 [03] WPIX
CR 1992-415712 [50]; 1997-107149 [10]; 1997-201472 [18]; 1997-271365 [24]; 1998-285799 [25]; 2002-265890 [31]; 2002-555994 [59]
DNN N1990-017092 DNC C1990-009978

TI Extraction of **endotoxin** binding protein from horseshoe crab amoebocytes - then purificn. by ultrafiltration and chromatography, useful in assay and therapeutic removal of **endotoxin**.

DC A89 B04 S03

IN **NOVITSKY, T J**; WAINWRIGHT, N R

PA **(ASCA-N) ASSOC CAPE COD INC**; **(ASCA-N) ASSOC OF CAPE COD**

CYC 14

PI WO-----8912644 A 19891228 (199003)* EN 58
RW: AT BE CH DE FR GB IT LU NL SE
W: AU JP
AU-----8937722 A 19900112 (199013)
EP------379549 A 19900801 (199031)
R: CH DE FR GB IT LI
JP----03501733 W 19910418 (199122)
EP------379549 A4 19920401 (199521)
EP------687911 A2 19951220 (199604) EN 22 G01N-033-579
R: AT BE CH DE FR GB IT LI LU NL SE
EP------379549 B1 19951227 (199605) EN 29 C07K-001-00
R: CH DE FR GB IT LI
DE----68925275 E 19960208 (199611) C07K-001-00
EP------687911 A3 19960821 (199641)
CA-----1338836 C 19970107 (199713) C07K-014-435
JP-----2774343 B2 19980709 (199832) 25 C07K-014-435
EP------687911 B1 20011017 (200169) EN G01N-033-579
R: AT BE CH DE FR GB IT LI LU NL SE
DE----68929334 E 20011122 (200201) G01N-033-579
DE----68929334 T2 20050818 (200554) G01N-033-579

ADT WO-----8912644 A 1989WO-US002665 19890621; EP------379549 A 1989EP-0907603 19890621; JP----03501733 W 1989JP-0506939 19890621; EP------379549 A4 1989EP-0907603 ; EP------687911 A2 1995EP-0201582 19890621; EP------379549 B1 1989EP-0907603 19890621, 1989WO-US02665 19890621; DE----68925275 E 1989DE-0625275 19890621, 1989EP-0907603 19890621, 1989WO-US02665 19890621; EP------687911 A3 Div ex 1989EP-0907603 19890621, 1995EP-0201582 19890621; CA-----1338836 C 1989CA-0604870 19890622; JP-----2774343 B2 1989JP-0506939 19890621, 1989WO-US02665 19890621; EP------687911 B1 Div ex 1989EP-0907603 19890621, 1995EP-0201582 19890621; DE----68929334 E 1989DE-0629334 19890621, 1995EP-0201582 19890621; DE----68929334 T2 1989DE-0629334 19890621, 1995EP-0201582 19890621

FDT EP------379549 B1 Based on WO-----8912644; DE----68925275 E Based on EP------379549, Based on WO-----8912644; JP-----2774343 B2 Previous Publ. JP----03501733, Based on WO-----8912644; EP------687911 B1 Div ex EP------379549; DE----68929334 E Based on EP------687911; DE----68929334 T2 Based on EP------687911

PRAI 1988US-0210575 19880623

REP 2.Jnl.Ref; US---4713347; US---4758655; US---4780529; 3.Jnl.Ref; 1.Jnl.Ref; No-SR.Pub; EP----224830; EP-----56210

IC A61K-037-02; C07K-003-28; C07K-015-08; G01N-027-26; G01N-033-56
ICM C07K-001-00; C07K-014-435; G01N-033-579
ICS A61K-035-56; A61K-037-02; A61K-038-00; B01D-061-14; B01J-020-26; C07K-001-14; C07K-001-16; C07K-001-18; C07K-001-20; C07K-001-34; C07K-003-28; C07K-015-08; G01N-027-26; G01N-027-327; G01N-030-88; G01N-033-56; G01N-033-567

AB WO 8912644 A UPAB: 20050823

Endotoxin binding protein (I) is isolated from a horseshoe crab by (1) lysing amoebocytes by hypotonic shock; (2) extracting recovered cell debris with a soln contg urea or guanidine hydrochloride as denaturant; (3) passing the extract through an ultrafiltration membrane with mol wt cut-off 20000-50000; (4) concn of the filtrate and passing through a second membrane with mol wt cut-off 5000-10000; (5) cation-exchange chromatography of the retentate at pH5-6; eluting with a urea-contg buffer, then (7) applying the (I)-contg peak to a reverse-phase column and recovering pure (I) with a buffer.

Amoebocytes are from **Limulus** polyphemus and are lysed in **endotoxin**-free water at 0-10 deg C. the cell debris is extracted with 6M denaturant soln and both ultrafiltration membranes are made of

polysulphone.
USE/ADVANTAGE - (I) binds **endotoxin** (II) so is useful in vivo (therapeutically or prophylactically) to reduce (II) concns eg in cases of septicaemia and toxic shock, and is normally administered intravenously at 100-1000 units/ng of measured (II) per day. It can also be used to remove (II) from protein solns or blood (in an extracorporeal system; pref when in immobilised form); for assaying (II), esp by measuring fluorescence emission from (I) before and after incubation with test sample; or, when immobilised on solid support, in biosensors.
Dwg.0/14
FS CPI EPI
FA AB
MC CPI: A05-J06; A12-W11A; A12-W11L; B04-B04A6; B12-J05; **B12-K04**
EPI: S03-E09C; S03-E14A; S03-E14H4

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(FILE 'HOME' ENTERED AT 13:33:40 ON 25 SEP 2006)

FILE 'WPIX' ENTERED AT 13:34:33 ON 25 SEP 2006
L1 3448 ENDOTOXIN? OR ENDO TOXIN?
L2 157 L1 AND LIMULUS?
L3 68633 (G01N033-48? OR G01N033-49? OR G01N033-50 OR G01N033-52 OR G01N
L4 66 (G01N033:48? OR G01N033:49? OR G01N033:50 OR G01N033:52 OR G01N
L5 245593 (SO3-E14H? OR D05-H04 OR D05-H09 OR B12-K04? OR C12-K04?)/MC OR
L6 127 L2 AND L3-5
L7 90 L6 NOT (PY>2003 OR AY>2003 OR PRY>2003)
E ASTRO C/AU
E CASTRO C/AU
L8 21 E3-4
E RIDGE R/AU
L9 7 E3,E5
E NOVITSKY T/AU
L10 13 E5
L11 14 (ASSOC? CAPE COD)/,CS,PA
E ASCA/PACO
E E3+ALL
L12 244 E1-2
L13 6 L6-7 AND L8-12
L14 86 L7 NOT L13
L15 1 L14 AND (GELCLOT? OR GEL CLOT?)
L16 7 L13,L15
L17 85 L14 NOT L16

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